09/980464

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=> d his

     (FILE 'HOME' ENTERED AT 12:14:19 ON 10 JUN 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:14:46 ON 10 JUN 2005
L1      1324738 S KINASE?
L2       395747 S LYMPH(A)NODE
L3        68040 S STROMAL(W)CELL
L4         5495 S L1 AND L2
L5          102 S L3 AND L4
L6      7110172 S CLON? OR EXPRESS? OR RECOMBINANT
L7           95 S L5 AND L6
L8           50 DUP REM L7 (45 DUPLICATES REMOVED)
L9      3990560 S MURINE OR MOUSE
L10           0 S L2(A)L3(A)L1
L11        1624 S L4 AND L9
L12          53 S L3 AND L11
L13          27 DUP REM L12 (26 DUPLICATES REMOVED)
                E BIRD T A/AU
L14         197 S E3
                E VIRCA G D/AU
L15         131 S E3
                E ANDERSON D M/AU
L16        1948 S E3
L17        2268 S L13 OR L14 OR L15 OR L16
L18          27 S L5 AND L17
L19          27 DUP REM L18 (0 DUPLICATES REMOVED)
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NEWS	4	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	5	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	6	FEB 28	MEDLINE/LMEDLINE reloaded
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NEWS	10	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	11	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	12	MAR 22	PATDPASPC - New patent database available
NEWS	13	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS	14	APR 04	EPFULL enhanced with additional patent information and new fields
NEWS	15	APR 04	EMBASE - Database reloaded and enhanced
NEWS	16	APR 18	New CAS Information Use Policies available online
NEWS	17	APR 25	Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.
NEWS	18	APR 28	Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus
NEWS	19	MAY 23	GBFULL enhanced with patent drawing images
NEWS	20	MAY 23	REGISTRY has been enhanced with source information from CHEMCATS
NEWS	21	MAY 26	STN User Update to be held June 6 and June 7 at the SLA 2005 Annual Conference
NEWS	22	JUN 06	STN Patent Forums to be held in June 2005
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=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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FILE 'LIFESCI' ENTERED AT 12:14:46 ON 10 JUN 2005
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=> s kinase?
L1     1324738 KINASE?

=> s lymph(a)node
L2      395747 LYMPH(A) NODE

=> s stromal(w)cell
   5 FILES SEARCHED...
L3       68040 STROMAL(W) CELL

=> s l1 and l2
L4        5495 L1 AND L2

=> s l3 and l4
L5         102 L3 AND L4

=> s clon? or express? or recombinant
   5 FILES SEARCHED...
L6     7110172 CLON? OR EXPRESS? OR RECOMBINANT
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=> s l5 and l6
L7 95 L5 AND L6

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8 50 DUP REM L7 (45 DUPLICATES REMOVED)

=> d 1-50 ibib ab

L8 ANSWER 1 OF 50 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:417298 SCISEARCH
THE GENUINE ARTICLE: 916SM
TITLE: **Expression** of CXCR4 and its down-regulation by IFN-gamma in head and neck squamous cell carcinoma
AUTHOR: Katayama A; Ogino T; Bandoh N; Nonaka S; Harabuchi Y (Reprint)
CORPORATE SOURCE: Asahikawa Med Coll, Dept Otolaryngol Head & Neck Surg, Midorigaoka Higashi 2-1-1-1, Asahikawa, Hokkaido 0788510, Japan (Reprint); Asahikawa Med Coll, Dept Otolaryngol Head & Neck Surg, Asahikawa, Hokkaido 0788510, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: CLINICAL CANCER RESEARCH, (15 APR 2005) Vol. 11, No. 8, pp. 2937-2946.
Publisher: AMER ASSOC CANCER RESEARCH, 615 CHESTNUT ST, 17TH FLOOR, PHILADELPHIA, PA 19106-4404 USA.
ISSN: 1078-0432.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 44

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Purpose: The functional **expression** of CXCR4, which plays roles in cell migration and proliferation in response to its unique ligand **stromal cell** - derived factor-1 (SDF-1), has been reported in variety of carcinomas. However, CXCR4 **expression** and its functional role in head and neck squamous cell carcinomas (HNSCC) remain unclear. In this study, we investigated CXCR4 **expression** and analyzed its functions in HNSCC cell lines. We also attempted to regulate CXCR4 **expression** using cytokines, such as interleukin-1, tumor necrosis factor-alpha, and IFN-gamma. Finally, we investigated correlation between CXCR4 **expression** and clinical features in patients with HNSCC.

Experimental Design: Six HNSCC cell lines were used in this study. Reverse transcription-PCR and flow cytometry analysis were shown for CXCR4 **expressions** with or without stimulations of cytokines. SDF-1-mediated cell migration was assayed in Matrigel-coated chemotaxis chamber. The SDF-1-mediated cell proliferation was analyzed by 3-(4,5-dimethylthiazol-2-yl) 2,E -diphenyltetrazolium bromide assay. The SDF-1-mediated signaling pathways were analyzed by Western blot analysis. Biopsy specimens from 56 patients with HNSCC were used for immunohistologic analysis.

Results: The significant CXCR4 **expression** was found in HSQ-89, IMC-3, and Nakamura cells. The SDF-1-mediated cell migration and proliferation were observed in CXCR4-positive cells. SDF-1 also promoted rapid phosphorylation of extracellular signal-regulated **kinase** 1/2 and Akt signaling pathways in CXCR4-positive cells. The SDF-1-mediated cell migration and proliferation of CXCR4-positive cells were inhibited by neutralization of CXCR4. Among three cytokines tested, IFN-gamma significantly reduced CXCR4 **expression** and SDF-1-induced cell migration and proliferation of CXCR4-positive cells. Immunohistologic analysis revealed that patients with advanced neck status and patients who developed distant metastases showed significantly higher CXCR4 **expression**, and the cause-specific survival of patients with

CXCR4-**expression** was significantly shorter. Furthermore, multivariate analysis confirmed that CXCR4 positive was the independent factor for cause-specific death.

Conclusion: Our results may provide an insight into future therapeutic agent that inhibits tumor metastasis and progression via down-regulating CXCR4 **expression** in patients with HNSCC.

L8 ANSWER 2 OF 50 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2005223785 EMBASE
TITLE: The role of CXCR4 in lung cancer metastasis and its possible mechanism.
AUTHOR: Su L.-P.; Zhang J.-P.; Xu H.-B.; Chen J.; Wang Y.; Xiong S.-D.
CORPORATE SOURCE: S.-D. Xiong, Department of Immunology, Shanghai Medical College of Fudan University, Shanghai 20032, China
SOURCE: National Medical Journal of China, (11 May 2005) Vol. 85, No. 17, pp. 1190-1194.
Refs: 16
ISSN: 0376-2491
COUNTRY: China
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: Chinese
SUMMARY LANGUAGE: Chinese; English
ENTRY DATE: Entered STN: 20050602
Last Updated on STN: 20050602

AB Objective: To investigate the role of CXCR4 in the metastasis of human lung cancer and its possible mechanism. Methods: Lung cancer cells of the lines 95C and 95D with high or low metastatic potential were transfeted with CXCR4 antisense plasmid pcDNA-ASX4, whole length eukaryotic **expression** plasmid pcDNA-CXCR4 (95D-ASX4 and 95C-X4 cell lines), and corresponding plasmid pcDNA3 (95C-pC and 95D-pC cell lines). 95C, 95C-pC, 95C-X4, 95D, and 95D-pC cells were injected subcutaneously into Balb/c nu/nu mice, 4 - 5 mice in a group. The mice were observed twice a week. Ten weeks later the mice were killed and the tumor in situ and the lungs were taken out to undergo histological examination. The effect of CXCR4 **expression** on the cell migration, MMP-2 activity, adhesion and GRO-a **expression** of lung cancer cells were detected by chemotaxis and chemoinvasion assay, zymography, adhesion assay and RT-PCR respectively. The polymerization of F-actin was measured by FACS and confocal microcopy. Western blotting was used to detect the phospharylation of ERK1/2 in 85D cells Results: Metastasis was not found in the mice injected with 95C and 95C-pC cells, and was seen in 2/5 of the mice injected with 95C-X4 cells, 3/4 of the mice injected with 95D and 95D-pC cells, 2/5 of the mice injected with 95D-ASX4 cells, however, the number of metastatic nodes in the lungs of 95D-ASX4 group was significantly less than those in the 95D and 95D-pC groups ($P = 0.044$). SDF-1a, a CXCR4 specific ligand, induced the migratory response and F-actin polymerization in the lung cancer cells; SDF-1a promoted the MMP-2 activity, the adhesion to vascular endothelial cells and GRO-a **expression**; and neutralizing CXCR4 antibody inhibited these effects to some degree. Moreover, SDF-1a induced the phosphorylation of ERK1/2 in human lung cancer cells. Conclusion: Metastasis of human lung cancer depends on, to some degree, the interaction of CXCR4 and SDF-1 that are involved in this process by regulating the active locomotion, MMP-2 activity, adhesion ability or GRO-a **expression**.

L8 ANSWER 3 OF 50 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN
ACCESSION NUMBER: 2005130488 EMBASE
TITLE: Breast cancer metastasis: When, where, how?.
AUTHOR: Eccles S.A.; Paon L.
CORPORATE SOURCE: S.A. Eccles, Cancer Res. UK Ctr. Cancer T., McElwain Laboratories, Institute of Cancer Research, Sutton, Surrey SM2 5NG, United Kingdom. Sue.Eccles@icr.ac.uk
SOURCE: Lancet, (19 Mar 2005) Vol. 365, No. 9464, pp. 1006-1007.
Refs: 8
ISSN: 0140-6736 CODEN: LANCAO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 20050407
Last Updated on STN: 20050407

L8 ANSWER 4 OF 50 EMBASE
on STN
ACCESSION NUMBER: 2005209199 EMBASE
TITLE: Tumor stroma interaction leading to the development of lethal phenotypes of human prostate cancer.
AUTHOR: Miyagi T.; Huang W.-C.; Sung S.-Y.; Zhau H.E.; Namiki M.; Chung L.W.K.
CORPORATE SOURCE: T. Miyagi, Department of Urology, Winship Cancer Institute, Emory University School of Medicine, Atlanta, GA 30322, United States
SOURCE: Nishinihon Journal of Urology, (2005) Vol. 67, No. 4, pp. 157-167.
Refs: 38
ISSN: 0029-0726 CODEN: NHJUAR
COUNTRY: Japan
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050526
Last Updated on STN: 20050526

AB Reciprocal tumor-stroma interactions between prostate cancer and bone **stromal cells** are crucial to the colonization and survival of prostate cancer cells in bone. Our ongoing investigations has shown that a number of soluble factors contribute to the interaction between prostate cancer, bone marrow **stromal cells**, osteoblasts, osteoclasts and vascular endothelial cells. Factors produced by prostate cancer and bone **stromal cells** could enhance osteoblastogenesis and/or osteoclastogenesis. The resulting activation of these responses could be the molecular basis of preferential prostate cancer homing and colonization in bone. Studying osteomimicry in prostate cancer cells, we identified novel cis-elements, CREs, that are responsible for mediating prostate cancer and bone stroma interaction with c-AMP-dependent PKA pathway, playing a pivotal role in the maintenance of bone-like properties by prostate cancer cells prior to metastasis. We identified a previously-identified factor in myeloma, β2M, as one of the key factors responsible for supporting osteomimicry of prostate cancer cells. By transfecting b2M into human prostate cancer cells, we observed explosive growth of human prostate cancer in bone. Since β2M is **expressed** by prostate cancer cells and clinical prostate tumors, and by a number of bone homing cancer types, we suggest that β2M is an attractive therapeutic target for the control of human prostate cancer bone metastasis.

L8 ANSWER 5 OF 50 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:371064 HCAPLUS
DOCUMENT NUMBER: 140:373461
TITLE: Evaluation of breast cancer states and outcomes using gene expression profiles
INVENTOR(S): West, Mike; Nevins, Joseph R.; Huang, Andrew
PATENT ASSIGNEE(S): Synpac, Inc., USA; Duke Univerisity
SOURCE: PCT Int. Appl., 799 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037996	A2	20040506	WO 2003-US33656	20031024
WO 2004037996	A3	20041229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004083084	A1	20040429	US 2002-291878	20021112
WO 2004044839	A2	20040527	WO 2002-US38216	20021112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004106113	A1	20040603	US 2002-291886	20021112

PRIORITY APPLN. INFO.:			
US 2002-420729P	P	20021024
US 2002-421062P	P	20021025
US 2002-421102P	P	20021025
US 2002-424701P	P	20021108
US 2002-424715P	P	20021108
US 2002-424718P	P	20021108
US 2002-291878	A	20021112
US 2002-291886	A	20021112
US 2002-425256P	P	20021112
WO 2002-US38216	A	20021112
WO 2002-US38222	A	20021112
US 2003-448461P	P	20030221
US 2003-448462P	P	20030221
US 2003-457877P	P	20030327
US 2003-458373P	P	20030331

AB The present invention relates generally to a method for evaluating and/or predicting breast cancer states and outcomes by measuring gene and metagene expression levels and integrating such data with clin. risk factors. Genes and metagenes whose expressions are correlated with a particular breast cancer risk factor or phenotype are provided using binary prediction tree modeling. The invention provides 175 genes associated

with metagene predictors of lymph node metastasis, 216 genes associated with metagene predictors of breast cancer recurrence, and 496 metagenes related to breast cancer study. Methods of using the subject genes and metagenes in diagnosis and treatment methods, as well as drug screening methods, etc are also provided. In addition, reagents, media and kits that find use in practicing the subject methods are also provided.

L8 ANSWER 6 OF 50 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:308529 HCAPLUS
DOCUMENT NUMBER: 140:333599
TITLE: Gene **expression** profile of human and mouse genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening
INVENTOR(S): Itoh, Mikito; Ogawa, Kaoru; Shinagawa, Akira; Sudo, Hajime; Ogawa, Hideoki; Ra, Chisei; Mitsuishi, Kouichi
PATENT ASSIGNEE(S): Genox Research, Inc., Japan; Juntendo University
SOURCE: PCT Int. Appl., 611 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004031386	A1	20040415	WO 2003-JP9808	20030801

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-229318 A 20020806
JP 2003-136543 A 20030514

AB This invention provides gene **expression** profile between a rash site and a no-rash site in a patient with atopic dermatitis or a patient with psoriasis. The invention also provides gene **expression** profile between a no-rash site in such a disease and a normal subject. Animal models, particularly mouse for those diseases are also claimed. The gene **expression** profile provided in this invention can be used for diagnosis, therapy, and drug screening for atopic dermatitis and psoriasis.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 50 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004627248 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15585839
TITLE: Intestinal cryptopatch formation in mice requires lymphotoxin alpha and the lymphotoxin beta receptor.
AUTHOR: Taylor Rebekah T; Lugering Andreas; Newell Kenneth A; Williams Ifor R
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, GA 30322, USA.
CONTRACT NUMBER: DK64399 (NIDDK)
DK64730 (NIDDK)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2004 Dec 15) 173 (12) 7183-9.
Journal code: 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20041220
Last Updated on STN: 20050209
Entered Medline: 20050208

AB Interactions between lymphotoxin (LT)alpha(1)beta(2) on inducer cells and the lymphotoxin beta receptor (LTbetaR) on **stromal cells** initiate development of **lymph nodes** and Peyer's patches. In this study, we assessed the contributions of LTalpha and LTbetaR to the development of cryptopatches (CP), aggregates of T cell precursors in the mouse small intestine. Mice genetically deficient in LTalpha or LTbetaR lacked CP. Bone marrow from LTalpha-deficient mice was unable to initiate development of CP or isolated lymphoid follicles (ILF) after transfer to CD132-null mice lacking CP and ILF. However, LTalpha-deficient bone marrow-derived cells contributed to CP formed in CD132-null mice receiving a mixture of wild-type and LTalpha-deficient bone marrow cells. Transfer of wild-type bone marrow into irradiated LTalpha-deficient mice resulted in reconstitution of both CP and ILF. However, the LT-dependent formation of CP was distinguished from the LT-dependent formation of ILF and Peyer's patches by not requiring the presence of an intact NF-kappaB-inducing **kinase** gene. CP but not ILF were present in the small intestine from NF-kappaB-inducing **kinase**-deficient alymphoplasia mice, indicating that the alternate NF-kappaB activation pathway required for other types of LTbetaR-dependent lymphoid organogenesis is dispensable for CP development. In addition, we identified VCAM-1(+) cells within both CP and ILF that are candidates for the **stromal cells** involved in receiving LT-dependent signals from the hemopoietic precursors recruited to CP. These findings demonstrate that interactions between cells **expressing** LTalpha(1)beta(2) and LTbetaR are a shared feature in the development of all small intestinal lymphoid aggregates.

L8 ANSWER 8 OF 50 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004572999 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15492752
TITLE: Acquisition of **lymph node**, but not distant metastatic potentials, by the overexpression of CXCR4 in human oral squamous cell carcinoma.
AUTHOR: Uchida Daisuke; Begum Nasima-Mila; Tomizuka Yoshifumi; Bando Takashi; Almofti Ammar; Yoshida Hideo; Sato Mitsunobu
CORPORATE SOURCE: Second Department of Oral and Maxillofacial Surgery, Tokushima University School of Dentistry, Kuramoto, Tokushima, Japan.. daisuke@dent.tokushima-u.ac.jp
SOURCE: Laboratory investigation; a journal of technical methods and pathology, (2004 Dec) 84 (12) 1538-46.
Journal code: 0376617. ISSN: 0023-6837.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20041117
Last Updated on STN: 20050422
Entered Medline: 20050421

AB Recently, it has been suggested that chemokine/receptor interactions determine the destination of the invasive tumor cells in several types of cancer. It has also been proposed that the **stromal cell** -derived factor-1 (SDF-1; CXCL12)/CXCR4 system might be involved **lymph node** metastasis in oral squamous cell carcinoma (SCC). In order to further clarify the role of the SDF-1/CXCR4 system in

oral SCC, we generated CXCR4 stable transfectants (IH-CXCR4) using oral SCC cells, and compared them to IH, which did not **express** CXCR4 and which did not have **lymph node** metastatic potentials in vivo. We introduced enhanced green fluorescent protein (GFP) fused-CXCR4 into IH cells, and detected the GFP fluorescence in the cytoplasm and cell membrane in approximately 60% of the G418-resistant cells. This bulk-transfectant **expressed** a high level of CXCR4 mRNA and protein, and exhibited the characteristic calcium fluxes and chemotactic activity observed in treatment with SDF-1. SDF-1 biphasically activated extracellular signal-regulated **kinase** (ERK)1/2, but continuously activated Akt/protein **kinase** B (PKB) in IH-CXCR4 cells. Most importantly, IH-CXCR4 cells frequently metastasized to the cervical **lymph node**, but not to the distant organs in the orthotopic inoculation of nude mice. Furthermore, these **lymph node** metastases were inhibited by the treatment of a mitogen-activated protein **kinase**/ERK **kinase** inhibitor, U0126, or a phosphatidylinositol 3 **kinase** inhibitor, wortmannin. These results indicate that SDF-1/CXCR4 signaling mediates the establishment of **lymph node** metastasis in oral SCC via ERK1/2 or Akt/PKB pathway.

L8 ANSWER 9 OF 50 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:954345 HCAPLUS
DOCUMENT NUMBER: 141:377496
TITLE: Ink4a/Arf **expression** is a biomarker of aging
AUTHOR(S): Krishnamurthy, Janakiraman; Torrice, Chad; Ramsey, Matthew R.; Kovalev, Grigoriy I.; Al-Regaiey, Khalid; Su, Lishan; Sharpless, Norman E.
CORPORATE SOURCE: Departments of Medicine and Genetics, The Lineberger Comprehensive Cancer Center, The University of North Carolina School of Medicine, Chapel Hill, NC, USA
SOURCE: Journal of Clinical Investigation (2004), 114(9), 1299-1307
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Ink4a/Arf locus encodes 2 tumor suppressor mols., p16INK4a and Arf, which are principal mediators of cellular senescence. To study the links between senescence and aging in vivo, we examined Ink4a/Arf **expression** in rodent models of aging. We show that **expression** of p16INK4a and Arf markedly increases in almost all rodent tissues with advancing age, while there is little or no change in the **expression** of other related cell cycle inhibitors. The increase in **expression** is restricted to well-defined compartments within each organ studied and occurs in both epithelial and **stromal cells** of diverse lineages. The age-associated increase in **expression** of p16INK4a and Arf is attenuated in the kidney, ovary, and heart by caloric restriction, and this decrease correlates with diminished **expression** of an in vivo marker of senescence, as well as decreased pathol. of those organs. Last, the age-related increase in Ink4a/Arf **expression** can be independently attributed to the **expression** of Ets-1, a known p16INK4a transcriptional activator, as well as unknown Ink4a/Arf coregulatory mols. These data suggest that **expression** of the Ink4a/Arf tumor suppressor locus is a robust biomarker, and possible effector, of mammalian aging.
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 50 MEDLINE on STN
ACCESSION NUMBER: 2004286637 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15186750

TITLE: Requirement for Tec **kinases** in chemokine-induced migration and activation of Cdc42 and Rac.
AUTHOR: Takesono Aya; Horai Reiko; Mandai Michiko; Dombroski Derek; Schwartzberg Pamela L
CORPORATE SOURCE: National Human Genome Research Institute, National Institutes of Health, Bethesda, MD 20892, USA.
SOURCE: Current biology : CB, (2004 May 25) 14 (10) 917-22. Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040610
Last Updated on STN: 20040721
Entered Medline: 20040720

AB Cell polarization and migration in response to chemokines is essential for proper development of the immune system and activation of immune responses. Recent studies of chemokine signaling have revealed a critical role for PI3-**Kinase**, which is required for polarized membrane association of pleckstrin homology (PH) domain-containing proteins and activation of Rho family GTPases that are essential for cell polarization and actin reorganization. Additional data argue that tyrosine **kinases** are also important for chemokine-induced Rac activation. However, how and which **kinases** participate in these pathways remain unclear. We demonstrate here that the Tec **kinases** Itk and Rlk play an important role in chemokine signaling in T lymphocytes. Chemokine stimulation induced transient membrane association of Itk and phosphorylation of both Itk and Rlk, and purified T cells from Rlk(-/-)Itk(-/-) mice exhibited defective migration to multiple chemokines in vitro and decreased homing to **lymph nodes** upon transfer to wt mice. **Expression** of a dominant-negative Itk impaired SDF-1alpha-induced migration, cell polarization, and activation of Rac and Cdc42. Thus, Tec **kinases** are critical components of signaling pathways required for actin polarization downstream from both antigen and chemokine receptors in T cells.

L8 ANSWER 11 OF 50 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004438925 EMBASE
TITLE: The chemokine network in cancer - Much more than directing cell movement.
AUTHOR: Kulbe H.; Levinson N.R.; Balkwill F.; Wilson J.L.
CORPORATE SOURCE: Dr. J.L. Wilson, Cancer Research UK, Translational Oncology Laboratory, Qu. Mary's Sch. of Med. and Dent., Charterhouse Square, London, EC1M 6BQ, United Kingdom. julia.wilson@cancer.org.uk
SOURCE: International Journal of Developmental Biology, (2004) Vol. 48, No. 5-6, pp. 489-496.
Refs: 83
ISSN: 0214-6282 CODEN: IJDBE5
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20041104
Last Updated on STN: 20041104

AB Cytokine and chemokine gradients are central to the directed movement of cells in both homeostatic and pathological processes. Most cancers have a

complex chemokine network which can influence immune responses to the tumor, direct the extent and cellular composition of the leukocyte infiltrate and also play a role in angiogenesis. Tumor cells can also hijack the chemokine system and gain **expression** of certain chemokine receptors and respond to specific chemokine gradients. Chemokine receptor **expression** and activation on malignant cells may be central to the growth, survival and migration of cancer cells from the primary tumor. Chemokine receptors, both CC and CXC have been detected on malignant cells and the relevant ligands are sometimes **expressed** at the tumor site and at sites of tumor spread, suggesting a role for the chemokine family in malignant growth and metastasis.

L8 ANSWER 12 OF 50 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2005194204 EMBASE
TITLE: CXCR4-SDF-1 signalling, locomotion, chemotaxis and adhesion.
AUTHOR: Kucia M.; Jankowski K.; Reca R.; Wysoczynski M.; Bandura L.; Allendorf D.J.; Zhang J.; Ratajczak J.; Ratajczak M.Z.
CORPORATE SOURCE: M.Z. Ratajczak, Stem Cell Biology Program, James Graham Brown Cancer Center, University of Louisville, Louisville, KY 40202, United States
SOURCE: Journal of Molecular Histology, (2004) Vol. 35, No. 3, pp. 233-245.
Refs: 111
ISSN: 1567-2379 CODEN: JMHOAO
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
026 Immunology, Serology and Transplantation
028 Urology and Nephrology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050526
Last Updated on STN: 20050526

AB Chemokines, small pro-inflammatory chemoattractant cytokines, that bind to specific G-protein-coupled seven-span transmembrane receptors present on plasma membranes of target cells are the major regulators of cell trafficking. In addition some chemokines have been reported to modulate cell survival and growth. Moreover, compelling evidence is accumulating that cancer cells may employ several mechanisms involving chemokine-chemokine receptor axes during their metastasis that also regulate the trafficking of normal cells. Of all the chemokines, stromal-derived factor-1 (SDF-1), an α-chemokine that binds to G-protein-coupled CXCR4, plays an important and unique role in the regulation of stem/progenitor cell trafficking. First, SDF-1 regulates the trafficking of CXCR4(+) haemato/lymphopoietic cells, their homing/retention in major haemato/lymphopoietic organs and accumulation of CXCR4(+) immune cells in tissues affected by inflammation. Second, CXCR4 plays an essential role in the trafficking of other tissue/organ specific stem/progenitor cells **expressing** CXCR4 on their surface, e.g., during embryo/organogenesis and tissue/organ regeneration. Third, since CXCR4 is **expressed** on several tumour cells, these CXCR4 positive tumour cells may metastasize to the organs that secrete/**express** SDF-1 (e.g., bones, **lymph nodes**, lung and liver).
SDF-1 exerts pleiotropic effects regulating processes essential to tumour metastasis such as locomotion of malignant cells, their chemoattraction and adhesion, as well as plays an important role in tumour vascularization. This implies that new therapeutic strategies aimed at blocking the SDF-1-CXCR4 axis could have important applications in the

clinic by modulating the trafficking of haemato/ lymphopoietic cells and inhibiting the metastatic behaviour of tumour cells as well. In this review, we focus on a role of the SDF-1-CXCR4 axis in regulating the metastatic behaviour of tumour cells and discuss the molecular mechanisms that are essential to this process. .COPYRGT. 2004 Kluwer Academic Publishers.

L8 ANSWER 13 OF 50 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004390846 EMBASE
TITLE: CXCR4-mediated adhesion and MMP-9 secretion in head and neck squamous cell carcinoma.
AUTHOR: Samara G.J.; Lawrence D.M.; Chiarelli C.J.; Valentino M.D.; Lyubsky S.; Zucker S.; Vaday G.G.
CORPORATE SOURCE: gayle.vaday@med.va.gov
SOURCE: Cancer Letters, (28 Oct 2004) Vol. 214, No. 2, pp. 231-241. Refs: 33
ISSN: 0304-3835 CODEN: CALEDQ
PUBLISHER IDENT.: S 0304-3835(04)00372-6
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 011 Otorhinolaryngology
016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040930
Last Updated on STN: 20040930

AB The chemokine CXCL12 (SDF-1) and its receptor, CXCR4, have been implicated in organ-specific metastases of several malignancies. Head and neck squamous cell carcinoma (HNSCC) predominantly metastasizes to **lymph nodes**, and recent evidence has shown that CXCL12 stimulates HNSCC migration. We explored the potential role of CXCR4 in mediating other metastatic processes in HNSCC cells. CXCR4 mRNA and cell-surface **expression** was assessed in HNSCC cell lines. CXCR4 mRNA **expression** was detected in five HNSCC cell lines. Cell-surface CXCR4 was also detected in each of the HNSCC cell lines and in resected HNSCC tissues. CXCL12 induced rapid intracellular calcium mobilization in a metastatic HNSCC cell line (HN), as well as rapid phosphorylation of ERK-1/2. HNSCC cell adhesion to fibronectin and collagen was increased by CXCL12 treatment, while the addition of an inhibitor of ERK-1/2 signaling, PD98059, reduced the effects of CXCL12. CXCL12 also increased the active matrix metalloproteinase (MMP)-9 secreted. Thus, HNSCC cells **express** functional CXCR4 receptors that induce rapid intracellular signaling upon binding to CXCL12. Such binding leads to increased HNSCC cell adhesion and MMP secretion, suggesting that CXCR4 may be a novel regulator of HNSCC metastatic processes. .COPYRGT. 2004 Elsevier Ireland Ltd. All rights reserved.

L8 ANSWER 14 OF 50 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:288935 BIOSIS
DOCUMENT NUMBER: PREV200400287692
TITLE: Differential TNFR and LT beta R regulation of High Endothelial Venule (HEV) Specific Genes.
AUTHOR(S): Liao, Shan [Reprint Author]; Lesslauer, Werner; Ruddle, Nancy H
CORPORATE SOURCE: Epidemiology and Public Health, Yale University School of Medicine, 60 College Street, New Haven, CT, 06520-8034, USA shan.liao@yale.edu
SOURCE: FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst. 332.1. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia,

USA. April 17-21, 2004. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jun 2004
Last Updated on STN: 16 Jun 2004

AB HEVs are specialized **lymph node** blood vessels where lymphocyte trafficking occurs. Optimal HEV function may be regulated at the level of gene **expression** of glycoproteins (GlyCAM-1, MAdCAM-1), chemokines (SLC) and posttranslational modifying enzymes (FucTIV, FucTVII, and an HEV specific GlcNAc-6-sulfotransferase (HEC-6ST)). We have previously determined that LTbR signaling contributes to HEV and HEC6ST in LTb-/- and in RIPLTab transgenic mice. Both the classical and alternative NF-kB pathways have been implicated in LTbR signal transduction in fibroblasts and spleen cells. However, it was not clear whether LTab could directly stimulate endothelial cells and/or whether its effect was mediated through **stromal cells**, which in turn activate HEV gene **expression**. Endothelial cell lines, bEND.3 and SVEC, were adopted as an in vitro system to evaluate and compare LTbR and TNFR mediated signaling for endothelial and HEV specific genes. FACS analysis revealed LTbR surface **expression** on both cell lines. Several genes were differentially induced by treatment with LTbR agonistic antibody or TNF. The signaling pathways regulating gene **expression** also differed as revealed by treatment with **kinase** or NF-kB inhibitors. Therefore, LTab has the capacity to directly activate endothelial cells and the pathways and genes differ from those employed by TNF. Supported by NIH CA16885 and the Anna Fuller Fund for Cancer Research. .

L8 ANSWER 15 OF 50 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003561148 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14633723
TITLE: Both hepatocyte growth factor (HGF) and stromal-derived factor-1 regulate the metastatic behavior of human rhabdomyosarcoma cells, but only HGF enhances their resistance to radiochemotherapy.
AUTHOR: Jankowski Kacper; Kucia Magda; Wysoczynski Marcin; Reca Ryan; Zhao Dongling; Trzyna Ela; Trent John; Peiper Stephen; Zembala Marek; Ratajczak Janina; Houghton Peter; Janowska-Wieczorek Anna; Ratajczak Mariusz Z
CORPORATE SOURCE: Stem Cell Biology Program, James Graham Brown Cancer Center, University of Louisville, 529 South Jackson Street, Louisville, KY 40202, USA.
CONTRACT NUMBER: 3P0 SE 10122 (NHLBI)
R01 HL 61796-01
SOURCE: Cancer research, (2003 Nov 15) 63 (22) 7926-35.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20031216
Last Updated on STN: 20040210
Entered Medline: 20040209

AB Rhabdomyosarcomas (RMSs) are frequently characterized by bone marrow involvement. Recently, we reported that human RMS cells **express** the CXC chemokine receptor-4 (CXCR4) and postulated a role for the CXCR4 stromal-derived factor (SDF)-1 axis in the metastasis of RMS cells to bone marrow. Because RMS cells also **express** the tyrosine **kinase** receptor c-MET, the specific ligand hepatocyte growth factor (HGF) that is secreted in bone marrow and **lymph**

node stroma, we hypothesized that the c-MET-HGF axis modulates the metastatic behavior of RMS cells as well. Supporting this concept is our observation that conditioned media harvested from expanded ex vivo human bone marrow fibroblasts chemoattracted RMS cells in an HGF- and SDF-1-dependent manner. Six human alveolar and three embryonal RMS cell lines were examined. We found that although HGF, similar to SDF-1, did not affect the proliferation of RMS cells, it induced in several of them: (a) locomotion; (b) stress fiber formation; (c) chemotaxis; (d) adhesion to human umbilical vein endothelial cells; (e) trans-Matrigel invasion and matrix metalloproteinase secretion; and (f) phosphorylation of mitogen-activated protein **kinase** p42/44 and AKT. Moreover HGF, but not SDF-1, increased the survival of RMS cells exposed to radio- and chemotherapy. We also found that the more aggressive alveolar RMS cells **express** higher levels of c-MET than embryonal RMS cell lines and "home/seed" better into bone marrow after i.v. injection into immunocompromised mice. Because we could not find any activating mutations in the **kinase** region of c-MET or any evidence for HGF autocrine stimulation, we suggest that the increased response of RMS cell lines depends on overexpression of functional c-MET. We conclude that HGF regulates the metastatic behavior of c-MET-positive RMS cells, directing them to the bone marrow and **lymph nodes**. Signaling from the c-MET receptor may also contribute to the resistance of RMS cells to conventional treatment modalities.

L8 ANSWER 16 OF 50 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-00219 BIOTECHDS
TITLE: Suppression of met **expression**: A possible cancer treatment;
potential prostate cancer gene therapy involving use of ribozyme against receptor protein-tyrosine-**kinase**
AUTHOR: SHINOMIYA N; WOUDE GFV
CORPORATE SOURCE: Van Andel Res Inst
LOCATION: Shinomiya N, Van Andel Res Inst, Oncol Mol Lab, 333 Bostwick NE, Grand Rapids, MI 49503 USA
SOURCE: CLINICAL CANCER RESEARCH; (2003) 9, 14, 5085-5090
ISSN: 1078-0432
DOCUMENT TYPE: Journal
LANGUAGE: English
AB DERWENT ABSTRACT: Met is a receptor protein-tyrosine-**kinase** (EC-2.7.1.112) and the only known receptor for HGF/SF. This ligand/receptor signaling pair mediates a vast range of biological activities not only in normal organ development and physiological functions but also in tumor proliferation, progression, invasion, and metastasis. Tumor cells that **express** high levels of Met molecules on their surface are more malignant and metastatic. In many carcinomas, HGF/SF acting in a paracrine manner is produced by **stromal cells** adjacent to the tumor. Inhibition of Met **expression** suppresses the malignant progression of tumor cells. A ribozyme strategy has been used to suppress the growth of human glioblastorna tumors. Because overexpression of Met receptors is observed in a wide spectrum of carcinomas and considered to play a key role in the progression of cancer cells, targeting of this molecule could become one of the most useful treatment modalities for refractory cancers. Molecular targeting of the Met signaling pathways by using specifically designed genes. which target c-met; can be used as a treatment modality for controlling tumor growth and metastasis. An adeno virus vector **expressing** c-Met ribozyme inhibits tumorigenicity and **lymph node** metastasis of human prostate cancer cells by using an orthotopically implanted in vivo mouse model. In prostate cancer cells especially, high **expression** of Met is associated with resistance against chemotherapy including hormonal therapy and is often observed in the advanced stages of clinical cases. By reducing Met **expression** using a ribozyme that targets Met mRNA, tumor growth

and **lymph node** metastasis were dramatically inhibited(6 pages)

L8 ANSWER 17 OF 50 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2003543598 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12881311
TITLE: Complexity within the plasma cell compartment of mice deficient in both E- and P-selectin: implications for plasma cell differentiation.
AUTHOR: Underhill Gregory H; Kolli K Pallav; Kansas Geoffrey S
CORPORATE SOURCE: Department of Microbiology-Immunology, Northwestern Medical School, 303 E Chicago Ave, Chicago, IL 60611, USA.
CONTRACT NUMBER: HL58710 (NHLBI)
SOURCE: Blood, (2003 Dec 1) 102 (12) 4076-83. Electronic Publication: 2003-07-24.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20031119
Last Updated on STN: 20040115
Entered Medline: 20040114

AB Antibody-secreting plasma cells represent the critical end-stage effector cells of the humoral immune response. Here, we show that several distinct plasma cell subsets are concurrently present in the **lymph nodes**, spleen, and bone marrow of mice deficient in both E- and P-selectin. One of these subsets was a B220-negative immunoglobulin g (IgG) plasma cell population **expressing** low to negative surface levels of syndecan-1. Examination of the chemotactic responsiveness of IgG plasma cell subsets revealed that migration toward **stromal cell**-derived factor 1/CXC ligand 12 (SDF-1/CXCL12) was primarily limited to the B220-lo subset regardless of tissue source. Although B220-negative plasma cells did not migrate efficiently in response to CXCL12 or to other chemokines for which receptor mRNA was **expressed**, these cells **expressed** substantial surface CXC chemokine receptor-4 (CXCR4), and CXCL12 stimulation rapidly induced extracellular signal regulated **kinase** 1 (ERK1)/ERK2 phosphorylation, demonstrating that CXCR4 retained signaling capacity. Therefore, B220-negative plasma cells exhibit a selective uncoupling of chemokine receptor **expression** and signaling from migration. Taken together, our findings document the presence of significant heterogeneity within the plasma cell compartment, which suggests a complex step-wise scheme of plasma cell differentiation in which the degree of differentiation and tissue location can influence the chemotactic responsiveness of IgG plasma cells.

L8 ANSWER 18 OF 50 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:330364 SCISEARCH
THE GENUINE ARTICLE: 664NP
TITLE: **Expression** of vascular endothelial growth factor (VEGF)-D and its receptor, VEGF receptor 3, as a prognostic factor in endometrial carcinoma
AUTHOR: Yokoyama Y (Reprint); Charnock-Jones D S; Licence D; Yanaihara A; Hastings J M; Holland C M; Emoto M; Sakamoto A; Sakamoto T; Maruyama H; Sato S; Mizunuma H; Smith S K
CORPORATE SOURCE: Hirosaki Univ, Sch Med, Dept Obstet & Gynecol, 5 Zaifu Cho, Hirosaki, Aomori 0368562, Japan (Reprint); Hirosaki Univ, Sch Med, Dept Obstet & Gynecol, Hirosaki, Aomori 0368562, Japan; Univ Cambridge, Dept Pathol, Reprod Mol Res Grp, Cambridge CB2 1QP, England

COUNTRY OF AUTHOR: Japan; England
SOURCE: CLINICAL CANCER RESEARCH, (APR 2003) Vol. 9, No. 4, pp. 1361-1369.
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202 USA.
ISSN: 1078-0432.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 43
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Purpose: To evaluate the prognostic value of vascular endothelial growth factor (VEGF)-D and VEGF receptor (VEGFR)-3 in endometrial carcinoma.

Experimental Design: We assessed the levels of immunoreactivity for VEGF-D and VEGFR-3 in 71 endometrial carcinomas, 14 complex atypical endometrial hyperplasias, and 16 normal endometria by immunohistochemistry.

Results: VEGF-D was stained in both tumor cells and adjacent **stromal cells**. VEGFR-3 was stained in both tumor cells and adjacent endothelial cells. Immunoreactivity for VEGF-D in tumor cells and adjacent **stromal cells** became significantly stronger as lesions progressed from normal endometrium to advanced carcinoma. Similarly, immunoreactivity for VEGFR-3 in tumor cells and adjacent endothelial cells was significantly greater as lesions progressed from normal endometrium to advanced carcinoma. A strong correlation was found between high levels of VEGF-D immunoreactivity in carcinoma cells and VEGFR-3 in both carcinoma cells and adjacent endothelial cells. Similarly, high levels of VEGF-D immunoreactivity in **stromal cells** were significantly correlated with those of VEGFR-3 in both carcinoma cells and endothelial cells. High levels of VEGF-D in carcinoma cells and **stromal cells**, as well as those of VEGFR-3 in carcinoma cells and endothelial cells, were significantly related to myometrial invasion and **lymph node** metastasis. A strong correlation was found between poor survival and high levels of VEGF-D in both carcinoma cells and **stromal cells** and between poor survival and high levels of VEGFR-3 in carcinoma cells. Moreover, the high levels of VEGF-D in **stromal cells** and VEGFR-3 in carcinoma cells were independent prognostic factors in endometrial carcinoma.

Conclusions: The presence of VEGF-D and VEGFR-3 in endometrial carcinoma may predict myometrial invasion and **lymph node** metastasis and may prospectively identify patients who are at increased risk for poor outcome. In addition, VEGF-D and VEGFR-3 may be promising targets for new therapeutic strategies in endometrial carcinoma.

L8 ANSWER 19 OF 50 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:451651 BIOSIS
DOCUMENT NUMBER: PREV200300451651
TITLE: Involvement of **stromal cell**-derived factor-1/CXCR4 signaling in **lymph node** metastasis of oral squamous cell carcinoma.
AUTHOR(S): Uchida, Daisuke [Reprint Author]; Begum, Nasima-Mila; Almofti, Ammar; Kawamata, Hitoshi; Nakashiro, Koh-Ichi; Tateishi, Yoshihisa; Hamakawa, Hiroyuki; Yoshida, Hideo; Sato, Mitsunobu
CORPORATE SOURCE: 2nd Dept. Oral and Maxillofacial Surgery, School of Dentistry, Tokushima University, Tokushima, Japan
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (July 2003) Vol. 44, pp. 452. print.
Meeting Info.: 94th Annual Meeting of the American Association for Cancer Research. Washington, DC, USA. July 11-14, 2003.

ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Oct 2003
Last Updated on STN: 1 Oct 2003

L8 ANSWER 20 OF 50 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:930083 SCISEARCH
THE GENUINE ARTICLE: 736BT
TITLE: Differential gene **expression** in pristane-induced arthritis susceptible DA versus resistant E3 rats
AUTHOR: Wester L (Reprint); Koczan D; Holmberg J; Olofsson P; Thiesen H J; Holmdahl R; Ibrahim S
CORPORATE SOURCE: Lund Univ, BMC, Biomed Ctr, Lund, Sweden (Reprint); Univ Rostock, Inst Immunol, Rostock, Germany
COUNTRY OF AUTHOR: Sweden; Germany
SOURCE: ARTHRITIS RESEARCH & THERAPY, (OCT 2003) Vol. 5, No. 6, pp. R361-R372.
Publisher: BIOMED CENTRAL LTD, MIDDLESEX HOUSE, 34-42 CLEVELAND ST, LONDON W1T 4LB, ENGLAND.
ISSN: 1478-6362.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Arthritis susceptibility genes were sought by analysis of differential gene **expression** between pristane-induced arthritis (PIA)-susceptible DA rats and PIA-resistant E3 rats. Inguinal **lymph nodes** of naive animals and animals 8 days after pristane injection were analyzed for differential gene **expression**. mRNA **expression** was investigated by microarray and real-time PCR, and protein **expression** was analyzed by flow cytometry or ELISA. Twelve genes were significantly differentially **expressed** when analyzed by at least two independent methods, and an additional five genes showed a strong a tendency toward differential **expression**. In naive DA rats IgE, the bone marrow **stromal cell** antigen 1 (Bst1) and the MHC class II beta-chain (MhcII) were **expressed** at a higher level, and the immunoglobulin kappa chain (Igkappa) was **expressed** at a lower level. In pristane-treated DA rats the MHC class II beta-chain, gelatinase B (Mmp9) and the protein tyrosine phosphatase CL100 (Ptpn16) were **expressed** at a higher level, whereas immunoglobulins, the CD28 molecule (Cd28), the mast cell specific protease 1 (Mcpt1), the carboxylesterase precursor (Ces2), K-cadherin (Cdh6), cyclin G1 (Ccng1), DNA polymerase IV (Primase) and the tumour associated glycoprotein E4 (Tage) were **expressed** at a lower level. Finally, the differentially **expressed** mRNA was confirmed with protein **expression** for some of the genes. In conclusion, the results show that animal models are well suited for reproducible microarray analysis of candidate genes for arthritis. All genes have functions that are potentially important for arthritis, and nine of the genes are located within genomic regions previously associated with autoimmune disease.

L8 ANSWER 21 OF 50 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2003491192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14567988
TITLE: Possible role of **stromal-cell**-derived factor-1/CXCR4 signaling on **lymph node** metastasis of oral squamous cell carcinoma.
AUTHOR: Uchida Daisuke; Begum Nasima Mila; Almofti Ammar; Nakashiro Koh-ichi; Kawamata Hitoshi; Tateishi Yoshihisa; Hamakawa

Hiroyuki; Yoshida Hideo; Sato Mitsunobu
CORPORATE SOURCE: Second Department of Oral and Maxillofacial Surgery, Tokushima University School of Dentistry, 3-18-15 Kuramoto, Tokushima 770-8504, Japan.. daisuke@dent.tokushima-u.ac.jp
SOURCE: Experimental cell research, (2003 Nov 1) 290 (2) 289-302. Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031022
Last Updated on STN: 20031219
Entered Medline: 20031202

AB We examined the role of chemokine signaling on the **lymph node** metastasis of oral squamous cell carcinoma (SCC) using **lymph node** metastatic (HNt and B88) and nonmetastatic oral SCC cells. Of 13 kinds of chemokine receptors examined, only CXCR4 **expression** was up-regulated in HNt and B88 cells. CXCR4 ligand, **stromal-cell**-derived factor-1alpha (SDF-1alpha; CXCL12), induced characteristic calcium fluxes and chemotaxis only in CXCR4-**expressing** cells. CXCR4 **expression** in metastatic cancer tissue was significantly higher than that in nonmetastatic cancer tissue or normal gingiva. Although SDF-1alpha was undetectable in either oral SCC or normal epithelial cells, submandibular **lymph nodes expressed** the SDF-1alpha protein, mainly in the **stromal cells**, but occasionally in metastatic cancer cells. The conditioned medium from lymphatic **stromal cells** promoted the chemotaxis of B88 cells, which was blocked by the CXCR4 neutralization. SDF-1alpha rapidly activated extracellular signal-regulated **kinase** (ERK)1/2 and Akt/protein **kinase** B (PKB), and their synthetic inhibitors attenuated the chemotaxis by SDF-1alpha. SDF-1alpha also activated Src family **kinases** (SFKs), and its inhibitor PP1 diminished the SDF-1alpha-induced chemotaxis and activation of both ERK1/2 and Akt/PKB. These results indicate that SDF-1/CXCR4 signaling may be involved in the establishment of **lymph node** metastasis in oral SCC via activation of both ERK1/2 and Akt/PKB induced by SFKs.

L8 ANSWER 22 OF 50 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2003125665 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12639303
TITLE: Phase I dose escalation clinical trial of adenovirus vector carrying osteocalcin promoter-driven herpes simplex virus thymidine **kinase** in localized and metastatic hormone-refractory prostate cancer.
AUTHOR: Kubo Hiroyuki; Gardner Thomas A; Wada Yoshitaka; Koeneman Kenneth S; Gotoh Akinobu; Yang Ling; Kao Chinghai; Lim So Dug; Amin Mahul B; Yang Hua; Black Margaret E; Matsubara Shigeji; Nakagawa Masayuki; Gillenwater Jay Y; Zhau Haiyen E; Chung Leland W K
CORPORATE SOURCE: Department of Urology, Winship Cancer Institute, Emory University School of Medicine, Atlanta, GA 30322, USA.
CONTRACT NUMBER: CA-79544-01A2 (NCI)
CA-85555 (NCI)
SOURCE: Human gene therapy, (2003 Feb 10) 14 (3) 227-41. Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030318
Last Updated on STN: 20031008
Entered Medline: 20031006

AB Osteocalcin (OC), a major noncollagenous bone matrix protein, is **expressed** prevalently in prostate cancer epithelial cells, adjacent fibromuscular **stromal cells**, and osteoblasts in locally recurrent prostate cancer and prostate cancer bone metastasis [Matsubara, S., Wada, Y., Gardner, T.A., Egawa, M., Park, M.S., Hsieh, C.L., Zhau, H.E., Kao, C., Kamidono, S., Gillenwater, J.Y., and Chung, L.W. (2001). Cancer Res. 61, 6012-6019]. We constructed an adenovirus vector carrying osteocalcin promoter-driven herpes simplex virus thymidine **kinase** (Ad-OC-hsv-TK) to cotarget prostate cancer cells and their surrounding **stromal cells**. A phase I dose escalation clinical trial of the intralesional administration of Ad-OC-hsv-TK followed by oral valacyclovir was conducted at the University of Virginia (Charlottesville, VA) in 11 men with localized recurrent and metastatic hormone-refractory prostate cancer (2 local recurrent, 5 osseous metastasis, and 4 **lymph node** metastasis) in order to determine the usefulness of this vector for the palliation of androgen-independent prostate cancer metastasis. This is the first clinical trial in which therapeutic adenoviruses are injected directly into prostate cancer **lymph node** and bone metastasis. Results show that (1). all patients tolerated this therapy with no serious adverse events; (2). local cell death was observed in treated lesions in seven patients (63.6%) as assessed by TUNEL assay, and histomorphological change (mediation of fibrosis) was detected in all posttreated specimens; (3). one patient showed stabilization of the treated lesion for 317 days with no alternative therapy. Of the two patients who complained of tumor-associated symptoms before the treatment, one patient with bone pain had resolution of pain, although significant remission of treated lesions was not observed by image examination; (4). CD8-positive T cells were predominant compared with CD4-positive T cells, B cells (L26 positive), and natural killer cells (CD56 positive) in posttreated tissue specimens; (5). levels of HSV TK gene transduction correlated well with coxsackie-adenovirus receptor **expression** but less well with the titers of adenovirus injected; and (6). intrinsic OC **expression** and the efficiency of HSV TK gene transduction affected the levels of HSV TK protein **expression** in clinical specimens. Our data suggest that this form of gene therapy requires further development for the treatment of androgen-independent prostate cancer metastasis although histopathological and immunohistochemical evidence of apoptosis was observed in the specimens treated. Further studies including the development of viral delivery will enhance the efficacy of Ad-OC-hsv-TK.

L8 ANSWER 23 OF 50 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:168136 BIOSIS
DOCUMENT NUMBER: PREV200400162042
TITLE: Synergistic effect of epidermal growth factor receptor and chemokine receptor CXCR4 in tumor metastasis.
AUTHOR(S): Wang, Zixuan [Reprint Author]; Dziedziejko, Violetta [Reprint Author]; Navenot, Jean-Marc D. [Reprint Author]; Peiper, Stephen C. [Reprint Author]
CORPORATE SOURCE: Department of Pathology, Medical College of Georgia, Augusta, GA, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 171b. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Mar 2004
Last Updated on STN: 24 Mar 2004

AB Elucidation of the fundamental mechanisms involved in tumor metastasis remains an important research priority and will lead to the development of novel treatment strategies. The major sites of breast cancer metastasis are regional **lymph nodes**, lung, liver, and bone marrow, and each has been shown to secrete **stromal cell** derived factor 1 (SDF-1), a member of the chemokine superfamily. The **expression** of CXCR4, the specific receptor for SDF-1 by breast cancer cell lines, and the finding that blockade of CXCR4 by its specific antibody inhibited metastatic spread in a xenograft model led to the recognition that a chemoattactant mechanism is involved in determining the organ-selective pattern of breast cancer metastases. Clinical data, on the other hand, indicate a strong association between activation of receptor tyrosine **kinases**, such as the epidermal growth factor (EGF) receptor (EGFR) and HER-2/neu, and the metastatic spread of tumor malignancy. To gain insight into the role of EGFR and CXCR4 in metastatic spread, HeLa cells that **express** functional CXCR4 and high levels of EGFR were used as a model of tumor cells in chemotaxis experiments. The chemotaxis of HeLa cells induced by SDF-1 was significantly increased when they were co-exposed to EGF, either in the top or bottom of standard transwell chambers. This synergism was completely inhibited by T140, a specific CXCR4 antagonist, or pertussis toxin. EGF alone induced chemokinesis, but not chemotaxis. Exposure of HeLa cells to EGF did not alter levels of CXCR4 on the cell surface. Since EGFR and CXCR4 signaling pathways both activate phosphatidylinositol 3-**kinase** (PI3-K), the induction of phosphorylation of Akt, a downstream target of this **kinase**, by SDF-1 in the presence and absence of EGF was determined by Western blotting. Cells incubated with both SDF-1 and EGF had a synergistic increase in Akt phosphorylation in comparison to those treated only with the chemokine or the growth factor. PI3-K antagonists blocked this effect and also inhibited directional migration of HeLa cells. These findings provide direct evidence for cross talk between RTK and GPCR pathways. They suggest that the role of CXCR4 in programming the metastatic spread of malignant cells may be regulated by RTKs. Thus, CXCR4 may be a suitable target for the blockade of metastatic spread in malignancies, particularly in those that overexpress RTKs.

L8 ANSWER 24 OF 50 MEDLINE on STN
ACCESSION NUMBER: 2003003088 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12393730
TITLE: CCR7-mediated physiological lymphocyte homing involves activation of a tyrosine **kinase** pathway.
AUTHOR: Stein Jens V; Soriano Silvia F; M'rini Christine; Nombela-Arrieta Cesar; de Buitrago Gonzalo Gonzalez; Rodriguez-Frade Jose Miguel; Mellado Mario; Girard Jean-Philippe; Martinez-A Carlos
CORPORATE SOURCE: Department of Immunology and Oncology, Centro Nacional de Biotecnologia/Consejo Superior de Investigaciones Cientificas (CSIC), Madrid, Spain.. jstein@cnb.uam.es
SOURCE: Blood, (2003 Jan 1) 101 (1) 38-44. Electronic Publication: 2002-06-28.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030103
Last Updated on STN: 20030331
Entered Medline: 20030318

AB Homing of blood-borne lymphocytes to peripheral **lymph nodes** (PLNs) is a multistep process dependent on the sequential engagement of L-selectin, which mediates lymphocyte rolling along the luminal surface of high endothelial venules (HEVs), followed by activation of lymphocyte integrins and transmigration through HEVs. Within lymphoid tissue, B and T lymphocytes then migrate toward specific microenvironments such as B-cell follicles and the paracortex, respectively. The lymphocyte-**expressed** chemokine receptor CCR7 is playing an important role during this process, as its HEV-presented ligands CCL19 and CCL21 can trigger rapid integrin activation under flow in addition to inducing a chemotactic response, which may participate in transmigration and/or interstitial migration. Here, we report that Tyrphostin (Tyr) AG490, a pharmacological inhibitor of Janus family tyrosine **kinases** (Jaks), blocked the chemotactic response of primary mouse lymphocytes to CCL19 and CCL21 in a dose-dependent manner. Furthermore, Tyr AG490 inhibited rapid CCL21-mediated up-regulation of alpha4 and beta2 integrin adhesiveness in static adhesion assays and under physiological flow, whereas adhesion induced by phorbol myristate acetate remained unaltered. Using intravital microscopy of subiliac PLNs in mice, we found that adoptively transferred Tyr AG490-treated lymphocytes adhered significantly less in HEVs compared with control cells, although L-selectin-mediated rolling was similar in both samples. Finally, we observed rapid Jak2 phosphorylation in CCL21-stimulated primary mouse lymphocytes. Thus, our study suggests a role for Jak tyrosine **kinases** during CCR7-mediated lymphocyte recirculation.

L8 ANSWER 25 OF 50 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:120036 HCAPLUS
DOCUMENT NUMBER: 138:236622
TITLE: RelB in secondary lymphoid organ development: differential regulation by lymphotoxin and tumor necrosis factor signaling pathways
AUTHOR(S): Yilmaz, Z. Buket
CORPORATE SOURCE: Institut fuer Toxikologie und Genetik, Germany
SOURCE: Wissenschaftliche Berichte - Forschungszentrum Karlsruhe (2002), FZKA 6793, i-xv, 1-117
CODEN: WBFKF5; ISSN: 0947-8620
DOCUMENT TYPE: Report
LANGUAGE: English

AB Primary lymphoid organs are the major sites of lymphopoiesis where lymphocytes proliferate and mature into functional but naive cells. Secondary lymphoid organs are sites where these lymphocytes encounter antigens and elicit immune responses. RelB is a member of the Rel/NF-κB family of inducible dimeric transcription factors. RelB is abundantly **expressed** in secondary lymphoid organs, such as spleen, **lymph nodes**, and Peyer's patches (PP). RelB-deficient mice have improper spleen structure and lack organizing centers for PPs, defects that can not be restored by the adoptive transfer of wild-type bone marrow cells. The work presented here revealed a reduction in **expression** of the homing chemokines B lymphocyte chemoattractant (BLC) and secondary lymphoid organ chemokine (SLC) in RelB-deficient spleen, suggesting a role for RelB in proper **expression** of chemokines by splenic **stromal cells**. Moreover, interleukin-7 (IL-7)-induced **expression** of lymphotoxin (LT) in intestinal cells, a crucial step in early PP development, was not impaired in RelB-deficient embryos, suggesting functional hematopoietic inducers and a defect in LTβ receptor (LTβR) **expressing** stromal responders. Activation of LTβR signaling in fibroblasts resulted in the specific induction of p52-RelB heterodimers, while tumor necrosis factor (TNF) induced classical p50-RelA NF-κB complexes. LTβR-induced RelB nuclear translocation and DNA binding of p52-RelB heterodimers required the

degradation of the inhibitory p52 precursor, p100, which was dependent on the IκB **kinase** (IKK) complex subunit IKKα, but not on IKKβ or IKKγ. In contrast to LTβR signaling, TNFR signaling increased p100 and RelB levels both in cytoplasm and nucleus and RelB was bound to p100 in both compartments. Despite the abundant presence of RelB in the nucleus, RelB DNA binding was almost undetectable in TNF treated fibroblasts. Forced **expression** of p50 and p52 could not rescue the lack of DNA binding. In contrast, RelB DNA binding increased in cells lacking the C-terminus of p100, but not of p105, strongly suggesting that it is the specific inhibitory function of the C-terminal domain of p100, rather than the lack of the heterodimerization partner, which prevents RelB DNA binding in TNF-stimulated fibroblasts. Thus, RelB and p52 in **stromal cells** could function in the proper development of the spleen by regulating the **expression** of chemokines such as BLC. Furthermore, generation of p52-RelB heterodimers by the LTβR pathway involving p100 degradation, appears to be a critical step in the formation of PP anlage.

REFERENCE COUNT: 118 THERE ARE 118 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 50 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:602742 BIOSIS
DOCUMENT NUMBER: PREV200200602742
TITLE: Regulation of cellular proliferation, cytoskeletal function, and signal transduction through CXCR4 and c-Kit in small cell lung cancer cells.
AUTHOR(S): Kijima, Takashi; Maulik, Gautam; Ma, Patrick C.; Tibaldi, Elena V.; Turner, Ross E.; Rollins, Barrett; Sattler, Martin; Johnson, Bruce E.; Salgia, Ravi [Reprint author]
CORPORATE SOURCE: Department of Adult Oncology, Dana-Farber Cancer Institute, 44 Binney Street, Dana 1234B, Boston, MA, 02115, USA ravi_salgia@dfci.harvard.edu
SOURCE: Cancer Research, (November 1, 2002) Vol. 62, No. 21, pp. 6304-6311. print.
CODEN: CNREA8. ISSN: 0008-5472.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Nov 2002
Last Updated on STN: 27 Nov 2002

AB The regulation of biological functions including cell growth, viability, migration, and adhesion of small cell lung cancer (SCLC) cells depends largely on the autocrine or paracrine stimulation of growth factor receptors and chemokine receptors. Stem cell factor (SCF) and its receptor c-Kit have been identified as important regulators of SCLC viability and are coexpressed in approximately 40-70% of SCLC specimens. In vitro, the inhibition of c-Kit tyrosine **kinase** activity by the small molecule tyrosine **kinase** inhibitor STI571 (Gleevec) abrogates cell growth. We have investigated the role of c-Kit and chemokine receptors in the regulation of cell migration and adhesion of SCLC cells. CXCR4, the chemokine receptor for **stromal cell**-derived factor-1alpha (SDF-1alpha), was found to be the major chemokine receptor commonly **expressed** in all of the 10 SCLC cell lines tested. SCF and SDF-1alpha increased cellular proliferation over a course of 72 h in both the c-Kit- and the CXCR4-positive NCI-H69 SCLC cell line. Recently, SDF-1alpha and CXCR4 have been shown to be important regulators of migration and metastasis in breast and ovarian cancer. We found that SDF-1alpha dramatically increased cell motility and adhesion in CXCR4-**expressing** NCI-H446 SCLC cells. In addition, SDF-1alpha altered cell morphology with increased formation of filopodia and neurite-like projections. In NCI-H69 SCLC cells, SCF and SDF-1alpha

cooperatively induced morphological changes and activated downstream signaling pathways. Treatment of NCI-H69 cells with STI571 specifically inhibited the c-Kit signaling events of Akt and p70 S6 **kinase**, whereas SDF-1alpha-mediated activation of Akt or p70 S6 **kinase** was normal. In contrast, the phosphatidylinositol 3-**kinase** inhibitor, LY294002, prevented these cells from adhering and completely blocked SCF- and/or SDF-1alpha-induced Akt or p70 S6 **kinase** phosphorylation. These results demonstrate that the CXCR4 receptor is functionally **expressed** in SCLC cells and may, therefore, be involved in the pathogenesis of SCLC in vivo. Inhibition of both the CXCR4 and the c-Kit downstream events could be a promising therapeutic approach in SCLC.

L8 ANSWER 27 OF 50 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2002496206 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12239174
TITLE: CXCR4-SDF-1 signaling is active in rhabdomyosarcoma cells and regulates locomotion, chemotaxis, and adhesion.
AUTHOR: Libura Jolanta; Drukala Justyna; Majka Marcin; Tomescu Oana; Navenot Jean Marc; Kucia Magda; Marquez Leah; Peiper Stephen C; Barr Frederic G; Janowska-Wieczorek Anna; Ratajczak Mariusz Z
CORPORATE SOURCE: Stem Cell Biology Program at the James Graham Brown Cancer Center, University of Louisville, KY 40202, USA.
CONTRACT NUMBER: 3P05E10122 (NHLBI)
R01 HL61796-01 (NCI)
R01CA64202
SOURCE: Blood, (2002 Oct 1) 100 (7) 2597-606.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021003
Last Updated on STN: 20021217
Entered Medline: 20021205

AB We hypothesized that the CXC chemokine receptor-4 (CXCR4)-stromal-derived factor-1 (SDF-1) axis may be involved in metastasis of CXCR4(+) tumor cells into the bone marrow and **lymph nodes**, which secrete the alpha-chemokine SDF-1. To explore this hypothesis, we phenotyped by fluorescence-activated cell sorter analysis various human tumor cell lines for **expression** of CXCR4 and found that it was highly **expressed** on several rhabdomyosarcoma (RMS) cell lines. We also observed that cell lines derived from alveolar RMS, which is characterized by recurrent PAX3- and PAX7-FKHR gene fusions and is associated with a poor prognosis, **expressed** higher levels of CXCR4 than lines derived from embryonal RMS. Furthermore, transfer of a PAX3-FKHR gene into embryonal RMS cell activates CXCR4 **expression** . Because alveolar RMS frequently metastasizes to the bone marrow and **lymph nodes**, it seems that the CXCR4-SDF-1 axis could play an important role in this process. These findings prompted us to determine whether SDF-1 regulates the metastatic behavior of RMS cells. Accordingly, we found that, although SDF-1 did not affect proliferation or survival of these cell lines, it induced in several of them (1) phosphorylation of mitogen-activated protein **kinase** p42/44; (2) locomotion; (3) directional chemotaxis across membranes covered by laminin, fibronectin, or Matrigel; (4) adhesion to laminin, fibronectin, and endothelial cells; and (5) increased MMP-2 and diminished tissue inhibitors of metalloproteinases secretion. The small-molecule CXCR4-specific inhibitor, T140, effectively blocked the in vitro responses of RMS cells to SDF-1. On the basis of these observations we suggest that the CXCR4-SDF-1 axis may play an important role in tumor spread and

metastasis of RMS cells to bone marrow and that molecular strategies aimed at inhibiting this axis could thus prove to be useful therapeutic measures.

L8 ANSWER 28 OF 50 MEDLINE on STN
ACCESSION NUMBER: 2002414602 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12168824
TITLE: **Expression** of the vascular endothelial growth factor receptor-3 (VEGFR-3) and its ligand VEGF-C in human colorectal adenocarcinoma.
AUTHOR: Witte Deborah; Thomas Abraham; Ali Najeeba; Carlson Nicole; Younes Mamoun
CORPORATE SOURCE: Department of Pathology, Baylor College of Medicine and The Methodist Hospital, Houston, TX 77030, USA.
SOURCE: Anticancer research, (2002 May-Jun) 22 (3) 1463-6. Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020810
Last Updated on STN: 20020914
Entered Medline: 20020913

AB Vascular endothelial growth factors (VEGF) are secreted by many tumor types, and are believed to affect tumor growth by promoting angiogenesis through binding to their receptors present on vascular endothelium. Recently, mRNA for VEGF-C the ligand for VEGFR-3, was found to be up-regulated in colorectal adenocarcinoma (CRC). The aim of this work was to determine: 1) the distribution of VEGF-C and VEGFR-3 in CRC, and 2) the biological significance of such **expression**. Sections of formalin-fixed and paraffin-embedded tissues from 56 CRC were immunohistochemically stained for VEGF-C and VEGFR-3. The type and percent of positive cells was recorded. Survival analysis was performed using the Kaplan-Meier method. All CRC were positive for VEGF-C which was present in the cancer cells themselves, as well as in **stromal cells**. Normal colon epithelium was usually negative. Only ten (17%) of the 56 CRC completely lacked VEGFR-3 **expression**. VEGFR-3 immunoreactivity was detected in <25% of the cancer cells in 22 cases and in >25% of the cells in 34 cases. **Expression** of VEGFR-3 in >25% of the cancer cells was associated with significantly poorer overall survival ($p<0.05$), but not with **lymph node** metastasis or depth of tumor invasion. Our results suggest that VEGFs promote cancer growth not only by stimulating angiogenesis, but also by acting on receptors present on the cancer cells themselves.

L8 ANSWER 29 OF 50 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2002454843 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12213723
TITLE: Tumor-associated macrophages **express** lymphatic endothelial growth factors and are related to peritumoral lymphangiogenesis.
AUTHOR: Schoppmann Sebastian F; Birner Peter; Stockl Johannes; Kalt Romana; Ullrich Robert; Caucig Carola; Kriehuber Ernst; Nagy Katalin; Alitalo Kari; Kerjaschki Dontscho
CORPORATE SOURCE: Department of Pathology, University of Vienna-Allgemeines Krankenhaus, Austria.
SOURCE: American journal of pathology, (2002 Sep) 161 (3) 947-56. Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020906
Last Updated on STN: 20020928
Entered Medline: 20020927

AB Formation of lymphatic metastasis is the initial step of generalized spreading of tumor cells and predicts poor clinical prognosis. Lymphatic vessels generally arise within the peritumoral stroma, although the lymphangiopoietic vascular endothelial growth factors (VEGF)-C and -D are produced by tumor cells. In a carefully selected collection of human cervical cancers (stage pT1b1) we demonstrate by quantitative immunohistochemistry and in situ hybridization that density of lymphatic microvessels is significantly increased in peritumoral stroma, and that a subset of **stromal cells express** large amounts of VEGF-C and VEGF-D. The density of cells producing these vascular growth factors correlates with peritumoral inflammatory stroma reaction, lymphatic microvessel density, and indirectly with peritumoral carcinomatous lymphangiosis and frequency of **lymph node** metastasis. The VEGF-C- and VEGF-D-producing stroma cells were identified in situ as a subset of activated tumor-associated macrophages (TAMs) by **expression** of a panel of macrophage-specific markers, including CD68, CD23, and CD14. These TAMs also **expressed** the VEGF-C- and VEGF-D-specific tyrosine **kinase** receptor VEGFR-3. As TAMs are derived from monocytes in the circulation, a search in peripheral blood for candidate precursors of VEGFR-3-**expressing** TAMs revealed a subfraction of CD14-positive, VEGFR-3-**expressing** monocytes, that, however, failed to **express** VEGF-C and VEGF-D. Only after in vitro incubation with tumor necrosis factor-alpha, lipopolysaccharide, or VEGF-D did these monocytes start to synthesize VEGF-C de novo. In conclusion VEGF-C-**expressing** TAMs play a novel role in peritumoral lymphangiogenesis and subsequent dissemination in human cancer.

L8 ANSWER 30 OF 50 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:274544 HCAPLUS
DOCUMENT NUMBER: 137:167190
TITLE: Activation of AKT/PKB in breast cancer predicts a worse outcome among endocrine treated patients
AUTHOR(S): Perez-Tenorio, G.; Stal, O.; Arnesson, L. G.; Malmstrom, A.; Nordenskjold, B.; Nordenskjold, K.; Bang, H.; Kallstrom, A. Ch.; Einarsson, E.; Norberg, B.; Skoog, P.; Henning, A.; Sundquist, M.; Tejler, G.
CORPORATE SOURCE: Southeast Sweden Breast Cancer Group, Department of Biomedicine and Surgery, Division of Oncology, Clinical Research Center, Faculty of Health Sciences, Linkoping University, Linkoping, SE-581 85, Swed.
SOURCE: British Journal of Cancer (2002), 86(4), 540-545
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Akt/PKB is a serine/threonine protein **kinase** that regulates cell cycle progression, apoptosis and growth factor mediated cell survival in association with tyrosine **kinase** receptors. The protein is a downstream effector of erbB-2 with implications in breast cancer progression and drug resistance in vitro. We aimed to examine the role of Akt-1 in breast cancer patients, by determing whether the **expression** (Akt-1) and/or activation (pAkt) were related to prognostic markers and survival. The **expression** of erbB-2, heregulin β1 and Bcl-2 was also assessed by flow cytometry or immunohistochem. This study comprised 93 patients, aged <50 who were treated with tamoxifen and/or goserelin. We found that pAkt was associated with lower S-phase fraction (P=0.001) and the presence of heregulin β1- **expressing stromal cells** (P=0.017).

Neither Akt-1 nor pAkt was related with other factors. Tumor cells-derived heregulin β1 was found mainly in estrogen receptor neg. (P=0.026) and node neg. (P=0.005) cases. Survival anal. revealed that pAkt pos. patients were more prone to relapse with distant metastasis, independently of S-phase fraction and nodal status (multivariate anal.; P=0.004). The results suggest that activation of Akt may have prognostic relevance in breast cancer.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 31 OF 50 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 9

ACCESSION NUMBER: 2002:901331 SCISEARCH
THE GENUINE ARTICLE: 609WR
TITLE: Activation of c-Src is inversely correlated with biological aggressiveness of breast carcinoma
AUTHOR: Ito Y; Kawakatsu H; Takeda T; Tani N; Kawaguchi N; Noguchi S; Sakai T; Matsuura N (Reprint)
CORPORATE SOURCE: Osaka Univ, Sch Allied Hlth Sci, Dept Pathol, Fac Med, 1-7 Yamadaoka, Suita, Osaka 5650871, Japan (Reprint); Osaka Univ, Sch Allied Hlth Sci, Dept Pathol, Fac Med, Suita, Osaka 5650871, Japan; Osaka Seamens Insurance Hosp, Dept Surg, Osaka, Japan; Univ Calif San Francisco, Lung Biol Ctr, San Francisco, CA 94143 USA; Osaka Univ, Sch Med, Dept Surg Oncol, Osaka, Japan; Lund Univ, Dept Expt Pathol, Lund, Sweden
COUNTRY OF AUTHOR: Japan; USA; Sweden
SOURCE: BREAST CANCER RESEARCH AND TREATMENT, (DEC 2002) Vol. 76, No. 3, pp. 261-267.
Publisher: KLUWER ACADEMIC PUBL, VAN GODEWIJCKSTRAAT 30, 3311 GZ DORDRECHT, NETHERLANDS.
ISSN: 0167-6806.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 39

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In order to investigate whether c-Src is involved in carcinogenesis and progression of breast carcinoma, we examined the **expression** of activated c-Src in tissue sections from surgically resected human breast specimens. First, we confirmed the specificity of the antibody against activated c-Src (**Clone** 28) using six cell lines established from human breast carcinomas by western blotting. As expected, activated c-Src was detected as a 60 kDa band in all cell lines tested. Immunofluorescence analysis demonstrated that the activated c-Src was mainly observed in cytoplasms of these cells. Then, we designed an immunohistochemical study with 73 human breast carcinoma tissues. Glandular epithelial and myoepithelial cells in normal mammary glands adjacent to carcinoma nests and infiltrating **stromal cells** were negative for activated c-Src. In contrast, 37 of the 73 breast carcinoma tested (50.7%) were positive for activated c-Src, and this positive staining was inversely correlated with Ki-67 labeling index ($p < 0.0001$), TNM stage ($p < 0.0001$), tumor size ($p < 0.0001$), and histological grade ($p = 0.0002$). These results strongly suggest that the activation of c-Src would be related to the progression of breast carcinomas with low aggressiveness.

L8 ANSWER 32 OF 50 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:73697 SCISEARCH
THE GENUINE ARTICLE: 509KH
TITLE: **Expression** and localization of vascular endothelial growth factor-C in rheumatoid arthritis synovial tissue
AUTHOR: Wauke K; Nagashima M (Reprint); Ishiwata T; Asano G;

Yoshino S

CORPORATE SOURCE: Nippon Med Coll, Dept Joint Dis & Rheumatism, Bunkyo Ku, 1-1-5 Sendagi, Tokyo 1138603, Japan (Reprint); Nippon Med Coll, Dept Joint Dis & Rheumatism, Bunkyo Ku, Tokyo 1138603, Japan; Nippon Med Coll, Dept Pathol, Bunkyo Ku, Tokyo 1138603, Japan

COUNTRY OF AUTHOR: Japan

SOURCE: JOURNAL OF RHEUMATOLOGY, (JAN 2002) Vol. 29, No. 1, pp. 34-38.
Publisher: J RHEUMATOL PUBL CO, 920 YONGE ST, SUITE 115, TORONTO, ONTARIO M4W 3C7, CANADA.
ISSN: 0315-162X.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 29

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Objective. Vascular endothelial growth factor-C (VEGF-C), a member of the VEGF family. induces lymphangiogenesis through VEGF receptor-3 (VEGFR-3/Flt-4). We examined the **expression** and localization of VEGF-C to clarify its role in synovial tissues in rheumatoid arthritis (RA).

Methods. Reverse transcription-polymerase chain reaction (RT-PCR), Western blot analysis, immunohistochemical staining, and in situ hybridization for VEGF-C were performed on synovial tissue specimens obtained from 10 patients with RA and 4 with osteoarthritis (OA), VEGFR-3 **expression** was determined using Western blot analysis.

Results. RT-PCR analysis showed that VEGF-C mRNA was **expressed** in all RA and OA synovial tissues. Based on Western blot analysis, the mature form of VEGF-C was round in RA synovial tissues, but not in OA synovial tissues, and VEGFR-3 was detected in RA and OA synovial tissues. Immunohistochemical staining showed that the VEGF-C protein was localized in many synovial lining cells, endothelial cells, and **stromal cells** in RA synovial tissues. In OA synovial tissues, the VEGF-C protein was localized in synovial lining cells and endothelial cells, A large number of synovial lining cells and **stromal cells** surrounding microvessels in RA synovial tissues **expressed** VEGF-C mRNA, as determined by in situ hybridization.

Conclusion. Mature VEGF-C and VEGFR-3 **expression** may contribute to lymphangiogenesis in RA.

L8 ANSWER 33 OF 50 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:164949 BIOSIS

DOCUMENT NUMBER: PREV200300164949

TITLE: VEGFR-3 in Cornea Lymphangiogenesis and APC Trafficking.

AUTHOR(S): Chen, L. [Reprint Author]; Hamrah, P. [Reprint Author]; Zhang, Q. [Reprint Author]; Dana, M. R. [Reprint Author]

CORPORATE SOURCE: Department of Ophthalmology, Schepens Eye Research Institute, Harvard Medical School, Boston, MA, USA

SOURCE: ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002, pp. Abstract No. 2268. cd-rom.
Meeting Info.: Annual Meeting of the Association For Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. May 05-10, 2002.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Apr 2003
Last Updated on STN: 2 Apr 2003

AB Purpose: Previous data from this lab indicate that lymphatic flow from the cornea to draining **lymph nodes** (LN) plays an important role in corneal immunity. Specifically, corneal transplantation to BALB/c hosts that had their cervical LN excised before surgery showed

indefinitely and universal graft acceptance (Yamagami S. & Dana M.R., 2001). VEGFR-3 (Flt-4) is a receptor tyrosine **kinase** which is mainly **expressed** on the lymphatic endothelium in adult tissues. The purpose of this study is to elucidate the **expressional** changes of VEGFR-3 during corneal neovascularization (NV) and its possible roles in cornea lymphangiogenesis and APC trafficking. Methods: Corneal NV was induced by intrastromal 11-0 nylon sutures in Balb/c mice. Eyes were procured 1, 3, 7, 14 days after the manipulation. Lymphatic vessels and VEGFR-3 positive cells were identified by confocal microscopy with immunofluorescence staining. Results: Cornea lymphatic vessels were detected with VEGFR-3 and CD31 double staining in corneal whole mounts starting at day 3 during induction of corneal NV. Cross sectional studies additionally revealed that the ocular surface epithelium of normal eyes **express** high levels of VEGFR-3. A sharp increase in VEGFR-3 staining in the corneal stroma was observed during the first week after induction of NV and a transient increase of VEGFR-3 **expression** on the epithelial layers of the limbus and conjunctival region around day 3 was also found. Additionally, corneal inflammation was associated with enhanced **expression** of VEGFR-3 by CD11c+ corneal dendritic cells. Conclusion: The **expression** of VEGFR-3 in the cornea and ocular surface is modified during corneal NV, both at the level of lymphatic vessels, and epithelial and **stromal cells**. These changes may affect trafficking of antigens and/or antigen-presenting cells from the eye to lymphoid organs and provide one explanation for why eyes with NV are considered 'high-risk' candidates for allograft survival. Additional studies including the use of **recombinant** VEGFR-3 chimeric protein in allograft cornea transplantation were undertaken to further define the possible functional roles of this receptor in lymphatic drainage and graft survival. Support: NIH/NEI Grant EY12963.

L8 ANSWER 34 OF 50 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:836585 HCAPLUS
DOCUMENT NUMBER: 136:353325
TITLE: PIP92 and NVM-1: Two genes associated with motility and metastasis
AUTHOR(S): Novac, Natalia
CORPORATE SOURCE: Inst. Toxikologie Genetik, Univ. Karlsruhe, Germany
SOURCE: Wissenschaftliche Berichte - Forschungszentrum Karlsruhe (2001), FZKA 6655, A, B, i-iii, iv-xvii, 1-165
CODEN: WBFKF5; ISSN: 0947-8620
DOCUMENT TYPE: Report
LANGUAGE: English

AB The differential screening method of Suppression Subtractive Hybridization (SSH) has previously been used to compare/identify genes associated with tumor progression and metastasis. More than a hundred genes were up-regulated in the highly metastatic cell line ASML in comparison to its non-metastatic counterpart IAS cells. In her thesis work the author has further differentially screened this group of genes to identify those that might play a role in the migration of metastasizing cells. This was achieved by analyzing the **expression** of these genes in mobilized and resident macrophages and in activated and non-activated lymphocytes. Those genes identified by these screens were then further screened for metastasis-related **expression** in multiple tumor models. Following this screening, two genes were selected for further characterization, Pip92 and NVM-1. Pip92 belongs to the "immediate early" gene family and has not previously been associated with tumor progression and metastasis. Its function is still obscure. To permit the functional anal. of the Pip92 protein polyclonal antibodies were generated. Pip92 has previously been shown by others to be cytoplasmic. However, the results obtained in the authors' work suggest that the Pip92 protein translocates to the nuclei for example upon serum stimulation. To get an

insight into the functional role of Pip92, the phenotype of IAS-Bsp73 cells stably overexpressing Pip92 protein was studied. IAS cells ectopically **expressing** the Pip92 protein exhibit enhanced motility in in vitro migration assays as compared to empty vector-transfected cells, suggesting that Pip92 might belong to the set of genes responsible for regulating cell migration. Properties of the Pip92 protein suggest it might act as a transcription regulatory protein and a search for genes whose **expression** is altered in Pip92-overexpressing cells was therefore performed. The **expression** of three genes was clearly up-regulated in cells overexpressing Pip92. The strongest induction was observed for osteopontin, a gene whose **expression** has previously been associated with migration and metastasis. Sections of human tumors dissected from patients with invasive ductal carcinoma were immunostained with the Pip92 antiserum. Pos. staining was observed only in tumor cells but not in non-neoplastic healthy tissues. NVM-1 (novel gene associated with metastasis) is a previously undescribed gene. Its full-length coding sequence was isolated and the predicted open reading frame was confirmed by an in vitro transcription/translation. The correlation of **expression** of NVM-1 with metastasis was confirmed in three tumor progression models in addition to one used for SSH. Upon completion of the human genome sequencing project it became apparent that the human homolog of NVM-1 (hNVM-1) gene is located on chromosome 14. The predicted amino acid sequence of hNVM-1 shows high homol. to the rat sequence. The genome sequence allowed the author to characterize the hNVM-1 promoter and the gene structure. Anal. of the hNVM-1 promoter revealed a number of potential transcription factor-binding sites within the putative hNVM-I promoter sequence. The hNVM-1 gene consists of 6 exons and 5 introns. A thorough computer anal. of the hNVM-1 gene structure and ESTs revealed the presence of two splice donor sites at the exon 2-intron 2 junction which are alternatively used in different tissues of human and rodent origin. Monoclonal antibodies against rNVM-I protein were generated and proved to be useful for Western Blot and immunohistochem. analyses, demonstrating a cytoplasmic location for the rNVM-I protein and **expression** of the protein in tumors. Further study of these genes may lead to the discovery of the new targets for antitumor drugs and may significantly help us to understand the process of transformation of nonmetastatic tumor cells into metastatic ones.

REFERENCE COUNT: 296 THERE ARE 296 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 35 OF 50 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:851435 HCAPLUS
DOCUMENT NUMBER: 136:1570
TITLE: Compositions, kits, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases associated therewith
INVENTOR(S): Hanrahan, Catherine F.; Feldman, Marc; Trepicchio, William L.
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA; Kennedy Institute of Rheumatology
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001088199	A2	20011122	WO 2001-US16022	20010517
WO 2001088199	A3	20030206		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2409154	AA	20011122	CA 2001-2409154	20010517
US 2002039734	A1	20020404	US 2001-860655	20010517
EP 1299560	A2	20030409	EP 2001-933353	20010517

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:	US 2000-205204P	P	20000518
	WO 2001-US16022	W	20010517

AB The invention relates to compns., kits and methods for identifying, detecting, and modulating the differentiation, growth, and/or maturation of Th1 or Th2 cells. The invention further relates to compns., kits, and methods for detecting, characterizing, preventing, and treating a Th1- or Th2-associated condition. A variety of markers are provided, wherein changes in the levels of **expression** of one or more of the markers is correlated with the presence of a Th1 or Th2 cell or Th1- or Th2-associated condition. Macrophage inhibitory factor (MIF) gene **expression** which is increased in both Th1-inducing and TH2-inducing condition is analyzed.

L8 ANSWER 36 OF 50 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER:	2001:159721 SCISEARCH
THE GENUINE ARTICLE:	400HY
TITLE:	**Expression** of the c-met proto-oncogene and its ligand, hepatocyte growth factor, in Hodgkin disease
AUTHOR:	Teofili L; Di Febo A L; Pierconti F; Maggiano N; Bendandi M; Rutella S; Cingolani A; Di Renzo N; Musto P; Pileri S; Leone G; Larocca L M (Reprint)
CORPORATE SOURCE:	Catholic Univ Sacred Heart, Inst Pathol, Largo F Vito 1, I-00168 Rome, Italy (Reprint); Catholic Univ Sacred Heart, Inst Pathol, I-00168 Rome, Italy; Catholic Univ Sacred Heart, Inst Hematol, I-00168 Rome, Italy; Catholic Univ Sacred Heart, Inst Infect Dis, I-00168 Rome, Italy; Casa Solievo Sofferenza, Div Hematol, Dept Onco Hematol, S Giovanni Rotondo, Italy; Univ Bologna, Inst Hematol Seragnoti, Bologna, Italy
COUNTRY OF AUTHOR:	Italy
SOURCE:	BLOOD, (15 FEB 2001) Vol. 97, No. 4, pp. 1063-1069. Publisher: AMER SOC HEMATOLOGY, 1900 M STREET. NW SUITE 200, WASHINGTON, DC 20036 USA. ISSN: 0006-4971.
DOCUMENT TYPE:	Article; Journal
LANGUAGE:	English
REFERENCE COUNT:	42

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The receptor for hepatocyte growth factor (HGF) is a transmembrane tyrosine **kinase** that is encoded by the proto-oncogene c-met Recently, c-MET was detected in Reed-Sternberg (RS) cells from Epstein-Barr virus-positive (EBV+) Hodgkin disease (HD). The c-MET, EBER-1, and LMP-1 **expression** in 45 **lymph node** biopsies and 12 bone marrow biopsies obtained from patients with HD was analyzed. In addition, HGF levels in serum samples from 80 healthy individuals and 135 HD patients in different phases of disease. In all 45 **lymph node** and 12 bone marrow samples examined, RS cells

expressed c-MET but not HGF(+). These results were independent of the EBV infection. Interestingly, several HGF+ dendritic-reticulum cells were found scattered around c-MET+ RS cells. The mean a SEM serum HGF levels in HD patients at diagnosis and at the time of relapse were 1403 +/- 91 (95% confidence interval [CI], 1221-1585) and 1497 +/- 242 pg/mL (95% CI, 977-2017), respectively. HGF values were significantly higher than those of healthy individuals (665 +/- 28 pg/mL; 95% CI, 600-721; and P < .001 for both groups of patients) and of HD patients in remission (616 +/- 49 pg/mL; 95% CI, 517-714; and P < .001 for both groups of patients). A significant correlation was found between serum HGF levels and B symptoms at diagnosis (P = .014). In conclusion, this study indicates that HGF and c-MET constitute an additional signaling pathway between RS cells and the reactive cellular background, thereby affecting adhesion, proliferation, and survival of RS cells. Furthermore, the serum concentration of HGF in HD patients may be a useful tool in monitoring the status of (C) 2001 by The American Society of Hematology.

L8 ANSWER 37 OF 50 MEDLINE on STN
ACCESSION NUMBER: 2001429559 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11477575
TITLE: Clinicopathological significance of vascular endothelial growth factor (VEGF)-C in human esophageal squamous cell carcinomas.
AUTHOR: Kitadai Y; Amioka T; Haruma K; Tanaka S; Yoshihara M; Sumii K; Matsutani N; Yasui W; Chayama K
CORPORATE SOURCE: Department of Endoscopy, Hiroshima University School of Medicine, Hiroshima, Japan.. ykitadai@mcai.med.hiroshima-u.ac.jp
SOURCE: International journal of cancer. Journal international du cancer, (2001 Sep 1) 93 (5) 662-6.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816

AB The purpose of this study was to investigate the **expression** of vascular endothelial growth factor (VEGF) -C in human esophageal squamous cell carcinomas to elucidate its role in **lymph node** metastasis and tumor progression. The **expression** of VEGF-C and flt-4 genes was examined in 5 esophageal carcinoma cell lines, 12 fresh biopsy specimens and 48 archival surgical specimens of human esophageal carcinoma tissues by RT-PCR and immunohistochemistry. Immunohistochemistry using antibodies against CD34 (endothelial cell specific) was also carried out and microvessels were quantified by counting vessels in a 200x field in the most vascular area of the tumor. Of the 5 human esophageal carcinoma cell lines, 4 constitutively **expressed** VEGF-C mRNA. In 8 (66.7%) of 12 cases, VEGF-C mRNA was detected in only tumor tissues but not in normal mucosa by RT-PCR. There was a significant relationship between VEGF-C and flt-4 mRNA **expression**. Out of the 48 surgical specimens of esophageal carcinomas, 19 (39.6%) and 10 (20.8%) exhibited intense VEGF-C immunoreactivity in the cytoplasm of many cancer cells and the **stromal cells**, respectively. In contrast, Flt-4 was mainly **expressed** on the lymphatic endothelial cells. Normal and dysplastic esophageal squamous epithelium exhibited no or faint cytoplasmic staining of VEGF-C. VEGF-C **expression** correlated with depth of tumor invasion, tumor stage, venous invasion, lymphatic invasion and **lymph node** metastasis. Vessel count was significantly higher in the VEGF-C positive tumors than in the negative

tumors. These results overall suggest that VEGF-C may play a role in tumor progression via lymphangiogenesis and angiogenesis in human esophageal carcinoma.

L8 ANSWER 38 OF 50 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2001357671 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11418238
TITLE: Identification of a new fibroblast growth factor receptor, FGFR5.
AUTHOR: Sleeman M; Fraser J; McDonald M; Yuan S; White D; Grandison P; Kumble K; Watson J D; Murison J G
CORPORATE SOURCE: Genesis Research and Development Corporation Ltd., 1 Fox Street, Parnell, Auckland, New Zealand.
SOURCE: Gene, (2001 Jun 27) 271 (2) 171-82.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF321300; GENBANK-AF321301
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010827
Last Updated on STN: 20010827
Entered Medline: 20010823

AB A novel fibroblast growth factor receptor (FGFR), designated FGFR5, was identified from an EST database of a murine **lymph node stromal cell** cDNA library. The EST has approximately 32% identity to the extracellular domain of FGFR1-4. Library screening with this EST identified two full-length alternative transcripts which we designated as FGFR5 beta and FGFR5 gamma. The main difference between these transcripts is that FGFR5 beta contains three extracellular Ig domains whereas FGFR5 gamma contains only two. A unique feature of FGFR5 is that it does not contain an intracellular tyrosine **kinase** domain. Predictive structural modelling of the extracellular domain of FGFR5 gamma suggested that it was a member of the I-set subgroup of the Ig-superfamily, consistent with the known FGFRs. Northern analysis of mouse and human FGFR5 showed detectable mRNA in a broad range of tissues, including kidney, brain and lung. Genomic sequencing identified four introns but identified no alternative transcripts containing a tyrosine **kinase** domain. Extracellular regions of FGFR5 beta and 5 gamma were **cloned** in-frame with the Fc fragment of human IgG(1) to generate **recombinant** non-membrane bound protein. **Recombinant** FGFR5 beta Fc and R5 gamma Fc demonstrated specific binding to the ligand FGF-2, but not FGF-7 or EGF. However, biological data suggest that FGF-2 binding to these proteins is with lower affinity than its cognate receptor FGFR2C. The above data indicate that this receptor should be considered as the fifth member of the FGFR family.

L8 ANSWER 39 OF 50 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:861815 HCAPLUS
DOCUMENT NUMBER: 134:26116
TITLE: Protein and cDNA sequences of human and mouse protein **kinase** sequence homologs, and uses thereof in identifying novel **kinase** inhibitor
INVENTOR(S): Bird, Timothy A.; Virca, G. Duke; Martin, Unja; Anderson, Dirk M.
PATENT ASSIGNEE(S): Immunex Corporation, USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073468	A1	20001207	WO 2000-US14696	20000526
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2374612	AA	20001207	CA 2000-2374612	20000526
EP 1181374	A1	20020227	EP 2000-939378	20000526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6514719	B1	20030204	US 2000-579664	20000526
US 2003162277	A1	20030828	US 2003-355975	20030130
US 6759223	B2	20040706		

PRIORITY APPLN. INFO.:	US 1999-136781P	P	19990528
	US 2000-579664	A3	20000526
	WO 2000-US14696	W	20000526

AB The invention is directed to purified and isolated novel murine and human **kinase** polypeptides, the nucleic acids encoding such polypeptides, processes for production of **recombinant** forms of such polypeptides, antibodies generated against these polypeptides, fragmented peptides derived from these polypeptides, and the uses of the above. Protein and cDNA sequences of novel human mouse protein **kinase** sequence homologs are identified by querying sequence data bases with DNA sequences from murine dendritic cell, murine **lymph node** **stromal cell**, human dendritic cell and human spleen cDNA library, using an algorithm designed to recognize **kinase** subdomains. The invention further relates to methods for identifying novel **kinase** inhibitor.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 40 OF 50 MEDLINE on STN DUPLICATE 11

ACCESSION NUMBER: 1999113739 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9916701
TITLE: Galectin-1 specifically modulates TCR signals to enhance TCR apoptosis but inhibit IL-2 production and proliferation.
AUTHOR: Vespa G N; Lewis L A; Kozak K R; Moran M; Nguyen J T; Baum L G; Miceli M C
CORPORATE SOURCE: Department of Microbiology and Immunology, University of California, Los Angeles, School of Medicine, 90095, USA.
CONTRACT NUMBER: CA-16042 (NCI)
R29 CA65979-01 (NCI)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1999 Jan 15) 162 (2) 799-806.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990223
Last Updated on STN: 19990223
Entered Medline: 19990208

AB Galectin-1 is an endogenous lectin **expressed** by thymic and

lymph node stromal cells at sites of Ag presentation and T cell death during normal development. It is known to have immunomodulatory activity in vivo and can induce apoptosis in thymocytes and activated T cells (1-3). Here we demonstrate that galectin-1 stimulation cooperates with TCR engagement to induce apoptosis, but antagonizes TCR-induced IL-2 production and proliferation in a murine T cell hybridoma and freshly isolated mouse thymocytes, respectively. Although CD4+ CD8+ double positive cells are the primary thymic subpopulation susceptible to galectin-1 treatment alone, concomitant CD3 engagement and galectin-1 stimulation broaden susceptible thymocyte subpopulations to include a subset of each CD4- CD8-, CD4+ CD8+, CD4- CD8+, and CD4+ CD8- subpopulations. Furthermore, CD3 engagement cooperates with suboptimal galectin-1 stimulation to enhance cell death in the CD4+ CD8+ subpopulation. Galectin-1 stimulation is shown to synergize with TCR engagement to dramatically and specifically enhance extracellular signal-regulated **kinase**-2 (ERK-2) activation, though it does not uniformly enhance TCR-induced tyrosine phosphorylation. Unlike TCR-induced IL-2 production, TCR/galectin-1-induced apoptosis is not modulated by the **expression** of **kinase** inactive or constitutively activated Lck. These data support a role for galectin-1 as a potent modulator of TCR signals and functions and indicate that individual TCR-induced signals can be independently modulated to specifically affect distinct TCR functions.

L8 ANSWER 41 OF 50 MEDLINE on STN
ACCESSION NUMBER: 1999341447 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10414497
TITLE: The **expression** of basic fibroblast growth factor (bFGF) in tumor-associated **stromal cells** and vessels is inversely correlated with non-small cell lung cancer progression.
AUTHOR: Guddo F; Fontanini G; Reina C; Vignola A M; Angeletti A; Bonsignore G
CORPORATE SOURCE: Institute of Lung Pathophysiology, National Research Council, Palermo, Italy.
SOURCE: Human pathology, (1999 Jul) 30 (7) 788-94.
Journal code: 9421547. ISSN: 0046-8177.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 20000303
Entered Medline: 19990803

AB Tumor progression results from complex interactions between tumor and tumor-associated host tissue. Basic fibroblast growth factor (bFGF), via activation of its receptor, FGFR-1, has been postulated to be an important inducer of host stromal response and angiogenesis. To assess the putative role of tumor-associated **stromal cells** and vessels in tumor progression, we studied non-small cell lung cancer (NSCLC) from 84 patients, including 51 squamous cell carcinomas and 33 nonsquamous cell carcinomas, by immunohistochemical detection. bFGF and FGFR-1 immunoreactivity was observed in tumor and in tumor-associated **stromal cells** and vessels. The **expression** of bFGF and FGFR-1 in **stromal cells** was higher in squamous than in non-squamous cell carcinomas (respectively, P = .007 and P = .0004). We found that bFGF and FGFR-1 **expression** in tumor and tumor-associated **stromal cells** and vessels was directly correlated with host stromal response, as assessed by intratumoral extension of stroma, but not with angiogenic response, as assessed by microvessel count. Although FGFR-1 **expression** of tumor cells was directly correlated with T-stage (P = .03), bFGF

expressions of tumor-associated **stromal cells** and vessels were inversely correlated with **lymph node** metastasis (respectively, P = .0001 and P = .0002) and advanced pathological stage (respectively, P = .03 and P = .01). These findings suggest that bFGF might mediate host stromal response in NSCLC and that the **expression** of bFGF in tumor-associated **stromal cells** and vessels might have an inhibitory role in NSCLC progression.

L8 ANSWER 42 OF 50 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:546891 SCISEARCH
THE GENUINE ARTICLE: ZZ446
TITLE: Binding of human immunodeficiency virus type 1 to CD4 and CXCR4 receptors differentially regulates **expression** of inflammatory genes and activates the MEK/ERK signaling pathway
AUTHOR: Popik W; Hesselgesser J E; Pitha P M (Reprint)
CORPORATE SOURCE: JOHNS HOPKINS UNIV, SCH MED, CTR ONCOL, 418 N BOND ST, BALTIMORE, MD 21231 (Reprint); JOHNS HOPKINS UNIV, SCH MED, CTR ONCOL, BALTIMORE, MD 21231; JOHNS HOPKINS UNIV, SCH MED, DEPT MOL & GENET, BALTIMORE, MD 21231; BERLEX BIOSCI, DEPT IMMUNOL, RICHMOND, CA 94804
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF VIROLOGY, (AUG 1998) Vol. 72, No. 8, pp. 6406-6413.
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0022-538X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 60

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have previously shown that binding of human immunodeficiency virus type 1 (HIV-1) virions to CD4 receptors stimulates association of Lck with Raf-1 and results in the activation of Raf-1 **kinase** in a Ras-independent manner. In the present study, we demonstrate that HIV-1 envelope glycoproteins of both T-cell-tropic and macrophagetropic strains rapidly activate the ERK/mitogen-activated protein (MAP) **kinase** pathway and the binding of nuclear transcription factors (AP-1, NF-kappa B, and C/EBP) and stimulate **expression** of cytokine and chemokine genes. The activation of this signaling pathway requires functional CD4 receptors and is independent of binding to CXCR4. Binding of the natural ligand **stromal cell**-derived factor 1 (SDF-1) to CXCR4, which inhibits entry of T-cell-tropic HIV-1, activates also the ERK/MAP **kinase** pathway. Bow ever, SDF-1 did not affect the CD4-mediated **expression** of cytokine and chemokine genes. These results provide firm molecular evidence that binding of HIV-1 envelope glycoproteins to CD4 receptor initiates a signaling pathway(s) independent of the binding to the chemokine receptor that leads to the aberrant **expression** of inflammatory genes and may contribute significantly to HIV-1 replication as well as to deregulation of the immune system.

L8 ANSWER 43 OF 50 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:776422 HCAPLUS
DOCUMENT NUMBER: 130:166834
TITLE: Regulation of adhesion and migration in the germinal center microenvironment
AUTHOR(S): Pals, Steven T.; Taher, Taher E. I.; Van Der Voort, Robbert; Smit, Lia; Keehnen, Robert M. J.
CORPORATE SOURCE: Department of Pathology, Academic Medical Center, University of Amsterdam, Amsterdam, 1105 AZ, Neth.

SOURCE: Cell Adhesion and Communication (1998), 6(2-3), 111-116
CODEN: CADCEF; ISSN: 1061-5385
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 67 refs. T cell dependent humoral immune responses are initiated by the activation of naive B cells in the T cell areas of the secondary lymphoid tissues. This primary B cell activation leads to migration of germinal center (GC) cell precursors into B cell follicles where they engage follicular dendritic cells (FDC) and T cells, and differentiate into memory B cells or plasma cells. Both B cell homing to the GC and interaction with FDC critically depend on integrin-mediated adhesion. We have recently identified the c-met-encoded receptor tyrosine **kinase** and its ligand, the growth and motility factor hepatocyte growth factor/scatter factor (HGF/SF), as a novel paracrine signaling pathway regulating B cell adhesion. The c-Met protein is **expressed** on B cells localized in the dark zone of the GC (centroblasts) and is induced by CD40 plus BCR ligation. Stimulation of c-Met with HGF/SF, which is produced at high levels by tonsillar **stromal cells** and FDC, leads to receptor phosphorylation and to enhanced integrin-mediated adhesion of B cells to both VCAM-1 and fibronectin. Interestingly, these responses to HGF/SF are promoted by heparan-sulfate proteoglycan forms of CD44 (CD44-HS). Like c-Met, CD44-HS is induced on B cells by CD40 ligation. It efficiently binds HGF/SF and strongly promotes signaling through c-Met. We conclude that integrin regulation during antigen specific B cell differentiation involves cross-talk between the HGF/SF-c-Met pathway and CD44-HS.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 44 OF 50 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:403715 HCAPLUS
DOCUMENT NUMBER: 127:134638
TITLE: Paracrine regulation of germinal center B cell adhesion through the c-Met-hepatocyte growth factor/scatter factor pathway
AUTHOR(S): van der Voort, Robbert; Taher, Taher E. I.; Keehnen, Robert M. J.; Smit, Lia; Groenink, Martijn; Pals, Steven T.
CORPORATE SOURCE: Dep. Pathology, Academic Med. Center, Univ. Amsterdam, Amsterdam, Neth.
SOURCE: Journal of Experimental Medicine (1997), 185(12), 2121-2131
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB T cell-dependent humoral immune responses are initiated by the activation of naive B cells in the T cell areas of the secondary lymphoid tissues. This primary B cell activation leads to migration of germinal center (GC) cell precursors into B cell follicles where they engage follicular dendritic cells (FDC) and T cells, and differentiate into memory B cells or plasma cells. Both B cell migration and interaction with FDC critically depend on integrin-mediated adhesion. To date, the physiol. regulators of this adhesion were unknown. Here, the authors have identified the c-met-encoded receptor tyrosine **kinase** and its ligand, the growth and motility factor hepatocyte growth factor/scatter factor (HGF/SF), as a novel paracrine signaling pathway regulating B cell adhesion. The authors observed that c-Met is predominantly **expressed** on CD38+CD77+ tonsillar B cells localized in the dark zone of the GC (centroblasts). On tonsil B cells, ligation of CD40 by CD40-ligand, induces a transient strong upregulation of **expression** of the

c-Met tyrosine **kinase**. Stimulation of c-Met with HGF/SF leads to receptor phosphorylation and, in addition, to enhanced integrin-mediated adhesion of B cells to both VCAM-1 and fibronectin. Importantly, the c-Met ligand HGF/SF is produced at high levels by tonsillar **stromal cells** thus providing signals for the regulation of adhesion and migration within the lymphoid microenvironment.

L8 ANSWER 45 OF 50 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 1998098359 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9436028
TITLE: Human prostate cancer progression models and therapeutic intervention.
AUTHOR: Chung L W; Kao C; Sikes R A; Zhau H E
CORPORATE SOURCE: Department of Urology, University of Virginia Health Sciences Center, Charlottesville, USA.
CONTRACT NUMBER: RO1 CA64863 (NCI)
SOURCE: Hinyokika kiyo. Acta urologica Japonica, (1997 Nov) 43 (11) 815-20. Ref: 12
Journal code: 0421145. ISSN: 0018-1994.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980306
Last Updated on STN: 19980306
Entered Medline: 19980224

AB Our laboratory has developed two cellular models of human prostate cancer progression. The LNCaP prostate cancer progression model is based upon the well-known cellular interaction between human prostate or bone **stromal cells** and LNCaP cells in vivo. The marginally tumorigenic LNCaP cells acquired tumorigenic and metastatic potential upon cellular interaction with either prostate or bone fibroblasts. A subline termed C4-2 was observed to grow readily in castrated animals and acquired metastatic potential spreading from the primary tumor site to the **lymph node**, the seminal vesicles, and the axial skeleton, resulting in an intense osteoblastic reaction. The second model is ARCaP, where prostate cancer cells derived from the ascites fluid of a man with metastatic disease exhibited an Androgen- and estrogen-Repressed Prostate Cancer cell growth and tumor formation in either a hormone-deficient or a castrated environment. However, the growth of either the tumor cells in vitro or the tumors in vivo was suppressed by both estrogen and androgen. While the tumor cells **expressed** low levels of androgen receptor and prostate-specific antigen (PSA), they were highly metastatic when inoculated orthotopically. Distant metastases to a number of organs were detected, including the liver, lung, kidney, and bone. We have employed a human prostate cancer progression model as a system to study the efficacy of gene therapy. Results of the study show that whereas universal promoters, such as Cytomegalovirus (CMV) and Rous Sarcoma Virus (RSV) promoter-driven tumor suppressors (e.g. p53, p21, and p16), were effective in inhibiting prostate tumor growth, the advantages of driving the **expression** of therapeutic toxic genes using a tissue-specific promoter prostate-specific antigen (PSA) and a tumor--but not tissue-specific promoter, osteocalcin (OC), are preferred. In the case of the PSA promoter, we can achieve cell-kill in PSA-producing human prostate cancer cells. To circumvent the supporting role of bone stroma for prostate cancer epithelial growth, we have recently developed a novel concept where the **expression** of therapeutic toxic genes is driven by a tumor--but not a tissue-specific OC promoter. Osteocalcin-thymidine **kinase** (OC-TK) was found to efficiently eradicate the growth of osteosarcoma, prostate, and brain tumors both in

vitro and in vivo. We observed that androgen-independent human prostate cancer cells lines **expressed** OC-TK at higher levels than androgen-dependent human prostate cancer cell lines. We have obtained data to suggest that Ad-OC-TK plus a pro-drug acyclovir (ACV) may be used as an effective therapy to treat prostate cancer bone metastasis in models where the growth of androgen-independent PC-3 and C4-2 tumors in the bone has occurred.

L8 ANSWER 46 OF 50 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 97122514 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8968108
TITLE: Induction of fibroblast gelatinase B **expression** by direct contact with cell lines derived from primary tumor but not from metastases.
AUTHOR: Segain J P; Harb J; Gregoire M; Meflah K; Menanteau J
CORPORATE SOURCE: Unite Institut National de la Sante et de la Recherche Medicale U 419,Institut de Biologie, Centre Hospitalier Universitaire, Nantes, France.
SOURCE: Cancer research, (1996 Dec 1) 56 (23) 5506-12. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 20000303
Entered Medline: 19970124

AB During cancer progression, tumor cells interact with **stromal cells**. As a consequence, matrix metalloproteinases are produced that contribute to the degradation of the extracellular matrix. This study used coculture systems to investigate fibroblast interaction with three colon cancer cell lines isolated from a single patient. Cells from primary colorectal carcinoma, but not from corresponding liver or **lymph node** metastases, induced gelatinase B **expression** by fibroblasts of different tissue origin. Remarkably, direct cell-cell contact was required for this induction, which occurred at the pretranslational level (as revealed by Northern blot analysis) and was completely blocked by anti-beta1 integrin monoclonal antibody, but only partially blocked by anti-alpha5 or anti-alpha(v). Induction was also inhibited by cytochalasin D, staurosporine, or dexamethasone, suggesting the need, respectively, for an organized actin cytoskeleton, protein **kinase** C, and AP-1-driven gene transcription. Our data suggest that direct tumor-**stromal cell** contact is one inductive event involved in matrix metalloproteinase **expression** by **stromal cells**.

L8 ANSWER 47 OF 50 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 14
ACCESSION NUMBER: 95155187 EMBASE
DOCUMENT NUMBER: 1995155187
TITLE: Involvement of CD45 in adhesion and suppression of apoptosis of mouse malignant T-lymphoma cells.
AUTHOR: Hanaoka K.; Fujita N.; Lee S.-H.; Seimiya H.; Naito M.; Tsuruo T.
CORPORATE SOURCE: Laboratory of Biomedical Research, Molecular/Cellular Biosciences Inst., University of Tokyo, 1-1-1, Yayoi,Bunkyo-ku, Tokyo 113, United States
SOURCE: Cancer Research, (1995) Vol. 55, No. 10, pp. 2186-2190. ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy

016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 950612
Last Updated on STN: 950612

AB Mouse malignant T-lymphoma CS-21 cells undergo apoptotic cell death in vitro in the absence of **lymph node stromal cells** but escape apoptosis and proliferate when they are attached to CA-12 **stromal cells**. A monoclonal antibody raised against CS-21 cell surface molecules (MCS-5) recognized a M(r) 168,000 protein, inhibited binding of CS-21 cells to CA-12 **stromal cells**, and suppressed apoptosis in CS-21 cells. To identify the M(r) 168,000 protein, we purified it with MCS-5 affinity chromatography and ion exchange chromatography. Partial amino acid sequences of the purified M(r) 168,000 protein were identical to those of CD45, a transmembrane tyrosine phosphatase. The purified protein possessed tyrosine phosphatase activity and was recognized by an anti-CD45 monoclonal antibody. The M(r) 168,000 protein was identified as CD45. To determine the CD45 isoform, we **cloned** the CD45 gene from the cDNA library of CS-21. Sixteen or 18 **clones** encoded CD45RO (CD45 lacking exons 4, 5, and 6), and the remainder lacked exons 4, 5, 6, and 7. Like MCS-5, an anti-CD45 monoclonal antibody, also inhibited binding of CS-21 cells to CA-12 cells and suppressed apoptosis in CS-21 cells. Our present results indicate that CD45RO **expressed** un CS-21 cells mediates adhesion to CA-12 cells and suppression of apoptosis.

L8 ANSWER 48 OF 50 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:491699 HCAPLUS
DOCUMENT NUMBER: 122:236647
TITLE: Apoptosis inhibition by anti-Mr 23,000 (Thy-1) monoclonal antibodies without inducing bcl-2 **expression**
AUTHOR(S): Fujita, Naoya; Naito, Mikihiko; Lee, Sang-Han; Hanaoka, Kenji; Tsuruo, Takashi
CORPORATE SOURCE: Inst. Molecular Cellular Biosciences, Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Cell Growth & Differentiation (1995), 6(4), 355-62
CODEN: CGDIE7; ISSN: 1044-9523
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mouse malignant T-lymphoma CS-21 cells grow in vitro in the presence of CA-12 **stromal cells**, but they undergo apoptotic cell death with DNA fragmentation when cultured alone. Because apoptosis of CS-21 cells was not inhibited by soluble factors secreted from CA-12 **stromal cells**, cell-cell interactions between the two seemed to be important to inhibit apoptosis. The authors found that CS-21 cell adhesion was mediated by Mr 168,000 and Mr 23,000 proteins and that apoptosis-inhibitory signals were transmitted through these proteins. In this study, the authors identified the Mr 23,000 cell adhesion mol. as a glycosylphosphatidylinositol-anchored Thy-1 (CD90) glycoprotein. Crosslinking of Mr 23,000 protein with anti-Mr 23,000 mAb and a second antibody transiently raised the [Ca2+]i and activated calcineurin in CS-21 cells, as has been observed in normal T lymphocytes stimulated by crosslinking anti-Thy-1 mAbs. However, differing from normal T lymphocytes, CS-21 cells could grow either by the transient increase in [Ca2+]i or by the activation of protein **kinase** C. Furthermore, Mr 23,000 protein-mediated cell survival of CS-21 cells was not accompanied by **expression** of the apoptosis-inhibiting protein bcl-2, although protein **kinase** C-activated cell survival was attended by bcl-2 **expression**. These results indicate that the Mr 23,000 protein (Thy-1) of CS 21 lymphoma cells functions as a cell adhesion mol. capable of transducing signals of cell survival and growth

that are not followed by bcl-2 **expression**.

L8 ANSWER 49 OF 50 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 95295089 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7539865
TITLE: c-met proto-oncogene **expression** in benign and malignant human prostate tissues.
AUTHOR: Pisters L L; Troncoso P; Zhau H E; Li W; von Eschenbach A C; Chung L W
CORPORATE SOURCE: Department of Urology, University of Texas M. D. Anderson Cancer Center, Houston 77030, USA.
CONTRACT NUMBER: R01-CA56307 (NCI)
R01-CA57361 (NCI)
R01-CA64863 (NCI)
+
SOURCE: Journal of urology, (1995 Jul) 154 (1) 293-8.
Journal code: 0376374. ISSN: 0022-5347.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199507
ENTRY DATE: Entered STN: 19950720
Last Updated on STN: 20000303
Entered Medline: 19950707

AB Previously, we demonstrated that hepatocyte growth factor/scatter factor (HGF/SF) is **expressed** by human bone **stromal cells** and is a powerful mitogen to prostatic epithelial cells in culture. Based on these observations, we hypothesized that, if prostate cancer cells in the prostate or bone environment respond to HGF/SF as a mitogen, then they must **express** the HGF/SF receptor, which is coded by the c-met proto-oncogene. We used immunohistochemical techniques to: 1) assess the presence and localization of c-met protein in benign and malignant human prostate tissues and 2) correlate the presence of c-met protein with tumor stage, grade and androgen sensitivity. c-met protein immunostaining was consistently observed in the basal epithelial layer of normal prostate glands but was absent in luminal epithelial cells of the peripheral and transition zones. c-met protein immunostaining was detected in 10 of 11 foci (91%) of high grade prostatic intraepithelial neoplasia (PIN). Overall, c-met protein staining was noted in 36 of 43 (84%) primary prostate cancer samples versus 2 of 11 (18%) benign prostate hyperplasia samples ($p < 0.0001$) and in 4 of 4 (100%) **lymph node** metastases, 23 of 23 (100%) bone marrow metastases and 1 of 3 (33%) other metastatic sites. There was a clear relationship between c-met protein staining and higher grade adenocarcinomas ($p < 0.001$). c-met protein is frequently detected in PIN and higher grade prostate cancers; future studies should evaluate the biological significance of these findings.

L8 ANSWER 50 OF 50 MEDLINE on STN
ACCESSION NUMBER: 95331136 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7607087
TITLE: Developmental **expression** of the mouse c-rel proto-oncogene in hematopoietic organs.
AUTHOR: Carrasco D; Weih F; Bravo R
CORPORATE SOURCE: Department of Molecular Biology, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, New Jersey 08543-4000, USA.
SOURCE: Development (Cambridge, England), (1994 Oct) 120 (10) 2991-3004.
Journal code: 8701744. ISSN: 0950-1991.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950828
Last Updated on STN: 20000303
Entered Medline: 19950814

AB We have studied the **expression** of the c-rel proto-oncogene during mouse embryonic development and adult animals using in situ hybridization and immunocytochemical analysis. c-rel transcripts were detected late in development with an **expression** pattern that parallels the emergence and diversification of hematopoietic cells. In the embryo, c-rel is **expressed** first in the mesoderm-derived hematopoietic cells of the liver and later also in other hematopoietic tissues such as thymus and spleen. This correlation between c-rel **expression** and places of hematopoietic infiltration is conserved in the postnatal period, with **expression** of c-rel mRNA in the medullary region of the thymus and in splenic B cell areas, including the marginal zone and the outer region of the periarterial sheath. High levels of c-rel transcripts were also detected in the splenic germinal centers, **lymph nodes** and Peyer's patches. Using double immunofluorescence and cell preparations from different embryonic and adult hematopoietic organs, we have defined the pattern and cell types of c-rel **expression** in different hematopoietic cell lineages and in the **stromal cell** content of the thymus. By using electrophoretic mobility shift assays, we have also correlated c-Rel **expression** in spleen with kappa B-binding activity in the form of c-Rel/p50 and c-Rel/p52 heterodimers.. The timing and pattern of **expression** of the c-rel proto-oncogene in the different cell lineages suggest that temporally regulated changes in c-Rel **expression** may be required for vertebrate hematopoiesis.

```
=> d his

     (FILE 'HOME' ENTERED AT 12:14:19 ON 10 JUN 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:14:46 ON 10 JUN 2005
L1      1324738 S KINASE?
L2       395747 S LYMPH(A)NODE
L3        68040 S STROMAL(W)CELL
L4         5495 S L1 AND L2
L5          102 S L3 AND L4
L6      7110172 S CLON? OR EXPRESS? OR RECOMBINANT
L7           95 S L5 AND L6
L8           50 DUP REM L7 (45 DUPLICATES REMOVED)

=> s murine or mouse
L9     3990560 MURINE OR MOUSE

=> s l2(a)l3(a)l1
L10           0 L2(A) L3(A) L1

=> s l4 and l9
L11        1624 L4 AND L9

=> s l3 and l11
L12          53 L3 AND L11

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13          27 DUP REM L12 (26 DUPLICATES REMOVED)
```

=> d 1-27 ibib ab

L13 ANSWER 1 OF 27 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:252300 SCISEARCH
THE GENUINE ARTICLE: 898JM
TITLE: Two distinctive pathways for recruitment of naive and primed IgM(+) B cells to the gut lamina propria
AUTHOR: Suzuki K; Meek B; Doi Y; Honjo T; Fagarasan S (Reprint)
CORPORATE SOURCE: RIKEN Res Ctr Allergy & Immunol, Tsurumi Ku, Kanagawa 2300045, Japan (Reprint); Kyoto Univ, Grad Sch Med, Dept Med Chem, Sakyo Ku, Kyoto 6068501, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (15 FEB 2005) Vol. 102, No. 7, pp. 2482-2486.
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418 USA.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 31
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Intestinal IgA(+) B cells are generated from IgM(+) B cells by in situ class switching in two separate gut microenvironments: organized follicular structures and lamina propria (LP). However, the origin of IgM(+) B cells in the gut LP is unknown. Transfer experiments to reconstitute IgM(+) B cells and IgA plasma cells in LP of aly/aly **mice**, which are defective in all organized follicular structures because of an NF-kappaB-inducing **kinase** (NIK) mutation, revealed that naive B cells can directly migrate to the LP. This migration requires NIK-dependent activation of gut **stromal cells**. By contrast, the entry of gut-primed IgM(+) B cells to the LIP is independent of **stromal cells** with functional NIK. Our results indicate that naive B cells directly migrate to the LIP by a distinct pathway from gut-primed B cells.

L13 ANSWER 2 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2005223785 EMBASE
TITLE: The role of CXCR4 in lung cancer metastasis and its possible mechanism.
AUTHOR: Su L.-P.; Zhang J.-P.; Xu H.-B.; Chen J.; Wang Y.; Xiong S.-D.
CORPORATE SOURCE: S.-D. Xiong, Department of Immunology, Shanghai Medical College of Fudan University, Shanghai 20032, China
SOURCE: National Medical Journal of China, (11 May 2005) Vol. 85, No. 17, pp. 1190-1194.
Refs: 16
ISSN: 0376-2491
COUNTRY: China
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: Chinese
SUMMARY LANGUAGE: Chinese; English
ENTRY DATE: Entered STN: 20050602
Last Updated on STN: 20050602

AB Objective: To investigate the role of CXCR4 in the metastasis of human lung cancer and its possible mechanism. Methods: Lung cancer cells of the

lines 95C and 95D with high or low metastatic potential were transfeted with CXCR4 antisense plasmid pcDNA-ASX4, whole length eukaryotic expression plasmid pcDNA-CXCR4 (95D-ASX4 and 95C-X4 cell lines), and corresponding plasmid pcDNA3 (95C-pC and 95D-pC cell lines). 95C, 95C-pC, 95C-X4, 95D, and 95D-pC cells were injected subcutaneously into Balb/c nu/nu **mice**, 4 - 5 **mice** in a group. The **mice** were observed twice a week. Ten weeks later the **mice** were killed and the tumor in situ and the lungs were taken out to undergo histological examination. The effect of CXCR4 expression on the cell migration, MMP-2 activity, adhesion and GRO-a expression of lung cancer cells were detected by chemotaxis and chemoinvasion assay, zymography, adhesion assay and RT-PCR respectively. The polymerization of F-actin was measured by FACS and confocal microcopy. Western blotting was used to detect the phospharylation of ERK1/2 in 85D cells Results: Metastasis was not found in the **mice** injected with 95C and 95C-pC cells, and was seen in 2/5 of the **mice** injected with 95C-X4 cells, 3/4 of the **mice** injected with 95D and 95D-pC cells, 2/5 of the **mice** injected with 95D-ASX4 cells, however, the number of metastatic nodes in the lungs of 95D-ASX4 group was significantly less than those in the 95D and 95D-pC groups (P = 0.044). SDF-1a, a CXCR4 specific ligand, induced the migratory response and F-actin polymerization in the lung cancer cells; SDF-1a promoted the MMP-2 activity, the adhesion to vascular endothelial cells and GRO-a expression; and neutralizing CXCR4 antibody inhibited these effects to some degree. Moreover, SDF-1a induced the phosphorylation of ERK1/2 in human lung cancer cells. Conclusion: Metastasis of human lung cancer depends on, to some degree, the interaction of CXCR4 and SDF-1 that are involved in this process by regulating the active locomotion, MMP-2 activity, adhesion ability or GRO-a expression.

L13 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:371064 HCAPLUS
DOCUMENT NUMBER: 140:373461
TITLE: Evaluation of breast cancer states and outcomes using gene expression profiles
INVENTOR(S): West, Mike; Nevins, Joseph R.; Huang, Andrew
PATENT ASSIGNEE(S): Synpac, Inc., USA; Duke Univerisity
SOURCE: PCT Int. Appl., 799 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037996	A2	20040506	WO 2003-US33656	20031024
WO 2004037996	A3	20041229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004083084	A1	20040429	US 2002-291878	20021112
WO 2004044839	A2	20040527	WO 2002-US38216	20021112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004106113	A1	20040603	US 2002-291886	20021112
PRIORITY APPLN. INFO.:			US 2002-420729P	P 20021024
			US 2002-421062P	P 20021025
			US 2002-421102P	P 20021025
			US 2002-424701P	P 20021108
			US 2002-424715P	P 20021108
			US 2002-424718P	P 20021108
			US 2002-291878	A 20021112
			US 2002-291886	A 20021112
			US 2002-425256P	P 20021112
			WO 2002-US38216	A 20021112
			WO 2002-US38222	A 20021112
			US 2003-448461P	P 20030221
			US 2003-448462P	P 20030221
			US 2003-457877P	P 20030327
			US 2003-458373P	P 20030331

AB The present invention relates generally to a method for evaluating and/or predicting breast cancer states and outcomes by measuring gene and metagene expression levels and integrating such data with clin. risk factors. Genes and metagenes whose expressions are correlated with a particular breast cancer risk factor or phenotype are provided using binary prediction tree modeling. The invention provides 175 genes associated with metagene predictors of **lymph node** metastasis, 216 genes associated with metagene predictors of breast cancer recurrence, and 496 metagenes related to breast cancer study. Methods of using the subject genes and metagenes in diagnosis and treatment methods, as well as drug screening methods, etc are also provided. In addition, reagents, media and kits that find use in practicing the subject methods are also provided.

L13 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:308529 HCAPLUS
DOCUMENT NUMBER: 140:333599
TITLE: Gene expression profile of human and **mouse** genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening
INVENTOR(S): Itoh, Mikito; Ogawa, Kaoru; Shinagawa, Akira; Sudo, Hajime; Ogawa, Hideoki; Ra, Chisei; Mitsuishi, Kouichi
PATENT ASSIGNEE(S): Genox Research, Inc., Japan; Juntendo University
SOURCE: PCT Int. Appl., 611 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004031386	A1	20040415	WO 2003-JP9808	20030801

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-229318 A 20020806
JP 2003-136543 A 20030514

AB This invention provides gene expression profile between a rash site and a no-rash site in a patient with atopic dermatitis or a patient with psoriasis. The invention also provides gene expression profile between a no-rash site in such a disease and a normal subject. Animal models, particularly **mouse** for those diseases are also claimed. The gene expression profile provided in this invention can be used for diagnosis, therapy, and drug screening for atopic dermatitis and psoriasis.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 27 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2004627248 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15585839
TITLE: Intestinal cryptopatch formation in **mice** requires lymphotoxin alpha and the lymphotoxin beta receptor.
AUTHOR: Taylor Rebekah T; Lugering Andreas; Newell Kenneth A; Williams Ifor R
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, GA 30322, USA.
CONTRACT NUMBER: DK64399 (NIDDK)
DK64730 (NIDDK)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2004 Dec 15) 173 (12) 7183-9.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20041220
Last Updated on STN: 20050209
Entered Medline: 20050208

AB Interactions between lymphotoxin (LT)alpha(1)beta(2) on inducer cells and the lymphotoxin beta receptor (LTbetaR) on **stromal cells** initiate development of **lymph nodes** and Peyer's patches. In this study, we assessed the contributions of LTalpha and LTbetaR to the development of cryptopatches (CP), aggregates of T cell precursors in the **mouse** small intestine. **Mice** genetically deficient in LTalpha or LTbetaR lacked CP. Bone marrow from LTalpha-deficient **mice** was unable to initiate development of CP or isolated lymphoid follicles (ILF) after transfer to CD132-null **mice** lacking CP and ILF. However, LTalpha-deficient bone marrow-derived cells contributed to CP formed in CD132-null **mice** receiving a mixture of wild-type and LTalpha-deficient bone marrow cells. Transfer of wild-type bone marrow into irradiated LTalpha-deficient **mice** resulted in reconstitution of both CP and ILF. However, the LT-dependent formation of CP was distinguished from the LT-dependent formation of ILF and Peyer's patches by not requiring the presence of an intact NF-kappaB-inducing **kinase** gene. CP but not ILF were present in the small intestine from NF-kappaB-inducing **kinase** -deficient alymphoplasia **mice**, indicating that the alternate NF-kappaB activation pathway required for other types of LTbetaR-dependent lymphoid organogenesis is dispensable for CP development. In addition, we identified VCAM-1(+) cells within both CP and ILF that are candidates for the **stromal cells** involved in receiving LT-dependent signals from the hemopoietic precursors recruited to CP. These findings

demonstrate that interactions between cells expressing LTalpha(1)beta(2) and LTbetaR are a shared feature in the development of all small intestinal lymphoid aggregates.

L13 ANSWER 6 OF 27 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004572999 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15492752
TITLE: Acquisition of **lymph node**, but not distant metastatic potentials, by the overexpression of CXCR4 in human oral squamous cell carcinoma.
AUTHOR: Uchida Daisuke; Begum Nasima-Mila; Tomizuka Yoshifumi; Bando Takashi; Almofti Ammar; Yoshida Hideo; Sato Mitsunobu
CORPORATE SOURCE: Second Department of Oral and Maxillofacial Surgery, Tokushima University School of Dentistry, Kuramoto, Tokushima, Japan.. daisuke@dent.tokushima-u.ac.jp
SOURCE: Laboratory investigation; a journal of technical methods and pathology, (2004 Dec) 84 (12) 1538-46. Journal code: 0376617. ISSN: 0023-6837.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20041117
Last Updated on STN: 20050422
Entered Medline: 20050421

AB Recently, it has been suggested that chemokine/receptor interactions determine the destination of the invasive tumor cells in several types of cancer. It has also been proposed that the **stromal cell** -derived factor-1 (SDF-1; CXCL12)/CXCR4 system might be involved **lymph node** metastasis in oral squamous cell carcinoma (SCC). In order to further clarify the role of the SDF-1/CXCR4 system in oral SCC, we generated CXCR4 stable transfectants (IH-CXCR4) using oral SCC cells, and compared them to IH, which did not express CXCR4 and which did not have **lymph node** metastatic potentials in vivo. We introduced enhanced green fluorescent protein (GFP) fused-CXCR4 into IH cells, and detected the GFP fluorescence in the cytoplasm and cell membrane in approximately 60% of the G418-resistant cells. This bulk-transfectant expressed a high level of CXCR4 mRNA and protein, and exhibited the characteristic calcium fluxes and chemotactic activity observed in treatment with SDF-1. SDF-1 biphasically activated extracellular signal-regulated **kinase** (ERK)1/2, but continuously activated Akt/protein **kinase** B (PKB) in IH-CXCR4 cells. Most importantly, IH-CXCR4 cells frequently metastasized to the cervical **lymph node**, but not to the distant organs in the orthotopic inoculation of nude **mice**. Furthermore, these **lymph node** metastases were inhibited by the treatment of a mitogen-activated protein **kinase**/ERK **kinase** inhibitor, U0126, or a phosphatidylinositol 3 **kinase** inhibitor, wortmannin. These results indicate that SDF-1/CXCR4 signaling mediates the establishment of **lymph node** metastasis in oral SCC via ERK1/2 or Akt/PKB pathway.

L13 ANSWER 7 OF 27 MEDLINE on STN
ACCESSION NUMBER: 2004286637 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15186750
TITLE: Requirement for Tec **kinases** in chemokine-induced migration and activation of Cdc42 and Rac.
AUTHOR: Takesono Aya; Horai Reiko; Mandai Michiko; Dombroski Derek; Schwartzberg Pamela L
CORPORATE SOURCE: National Human Genome Research Institute, National Institutes of Health, Bethesda, MD 20892, USA.
SOURCE: Current biology : CB, (2004 May 25) 14 (10) 917-22.

Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040610
Last Updated on STN: 20040721
Entered Medline: 20040720

AB Cell polarization and migration in response to chemokines is essential for proper development of the immune system and activation of immune responses. Recent studies of chemokine signaling have revealed a critical role for PI3-**Kinase**, which is required for polarized membrane association of pleckstrin homology (PH) domain-containing proteins and activation of Rho family GTPases that are essential for cell polarization and actin reorganization. Additional data argue that tyrosine **kinases** are also important for chemokine-induced Rac activation. However, how and which **kinases** participate in these pathways remain unclear. We demonstrate here that the Tec **kinases** Itk and Rlk play an important role in chemokine signaling in T lymphocytes. Chemokine stimulation induced transient membrane association of Itk and phosphorylation of both Itk and Rlk, and purified T cells from Rlk(-/-)Itk(-/-) **mice** exhibited defective migration to multiple chemokines in vitro and decreased homing to **lymph nodes** upon transfer to wt **mice**. Expression of a dominant-negative Itk impaired SDF-1alpha-induced migration, cell polarization, and activation of Rac and Cdc42. Thus, Tec **kinases** are critical components of signaling pathways required for actin polarization downstream from both antigen and chemokine receptors in T cells.

L13 ANSWER 8 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:288935 BIOSIS
DOCUMENT NUMBER: PREV200400287692
TITLE: Differential TNFR and LT beta R regulation of High Endothelial Venule (HEV) Specific Genes.
AUTHOR(S): Liao, Shan [Reprint Author]; Lesslauer, Werner; Ruddle, Nancy H
CORPORATE SOURCE: Epidemiology and Public Health, Yale University School of Medicine, 60 College Street, New Haven, CT, 06520-8034, USA shan.liao@yale.edu
SOURCE: FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst. 332.1. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia, USA. April 17-21, 2004. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jun 2004
Last Updated on STN: 16 Jun 2004

AB HEVs are specialized **lymph node** blood vessels where lymphocyte trafficking occurs. Optimal HEV function may be regulated at the level of gene expression of glycoproteins (GlyCAM-1, MAdCAM-1), chemokines (SLC) and posttranslational modifying enzymes (FucTIV, FucTVII, and an HEV specific GlcNAc-6-sulfotransferase (HEC-6ST)). We have previously determined that LTbR signaling contributes to HEV and HEC6ST in LTb-/- and in RIPLTab transgenic **mice**. Both the classical and alternative NF-kB pathways have been implicated in LTbR signal transduction in fibroblasts and spleen cells. However, it was not clear whether LTab could directly stimulate endothelial cells and/or whether its effect was mediated through **stromal cells**, which in turn activate HEV gene expression. Endothelial cell lines, bEND.3 and

SVEC, were adopted as an in vitro system to evaluate and compare LTbR and TNFR mediated signaling for endothelial and HEV specific genes. FACS analysis revealed LTbR surface expression on both cell lines. Several genes were differentially induced by treatment with LTbR agonistic antibody or TNF. The signaling pathways regulating gene expression also differed as revealed by treatment with **kinase** or NF-kB inhibitors. Therefore, LTab has the capacity to directly activate endothelial cells and the pathways and genes differ from those employed by TNF. Supported by NIH CA16885 and the Anna Fuller Fund for Cancer Research.

L13 ANSWER 9 OF 27 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003561148 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14633723
TITLE: Both hepatocyte growth factor (HGF) and stromal-derived factor-1 regulate the metastatic behavior of human rhabdomyosarcoma cells, but only HGF enhances their resistance to radiochemotherapy.
AUTHOR: Jankowski Kacper; Kucia Magda; Wysoczynski Marcin; Reca Ryan; Zhao Dongling; Trzyna Ela; Trent John; Peiper Stephen; Zembala Marek; Ratajczak Janina; Houghton Peter; Janowska-Wieczorek Anna; Ratajczak Mariusz Z
CORPORATE SOURCE: Stem Cell Biology Program, James Graham Brown Cancer Center, University of Louisville, 529 South Jackson Street, Louisville, KY 40202, USA.
CONTRACT NUMBER: 3P0 SE 10122 (NHLBI)
R01 HL 61796-01
SOURCE: Cancer research, (2003 Nov 15) 63 (22) 7926-35. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20031216
Last Updated on STN: 20040210
Entered Medline: 20040209

AB Rhabdomyosarcomas (RMSs) are frequently characterized by bone marrow involvement. Recently, we reported that human RMS cells express the CXC chemokine receptor-4 (CXCR4) and postulated a role for the CXCR4 stromal-derived factor (SDF)-1 axis in the metastasis of RMS cells to bone marrow. Because RMS cells also express the tyrosine **kinase** receptor c-MET, the specific ligand hepatocyte growth factor (HGF) that is secreted in bone marrow and **lymph node** stroma, we hypothesized that the c-MET-HGF axis modulates the metastatic behavior of RMS cells as well. Supporting this concept is our observation that conditioned media harvested from expanded ex vivo human bone marrow fibroblasts chemoattracted RMS cells in an HGF- and SDF-1-dependent manner. Six human alveolar and three embryonal RMS cell lines were examined. We found that although HGF, similar to SDF-1, did not affect the proliferation of RMS cells, it induced in several of them: (a) locomotion; (b) stress fiber formation; (c) chemotaxis; (d) adhesion to human umbilical vein endothelial cells; (e) trans-Matrigel invasion and matrix metalloproteinase secretion; and (f) phosphorylation of mitogen-activated protein **kinase** p42/44 and AKT. Moreover HGF, but not SDF-1, increased the survival of RMS cells exposed to radio- and chemotherapy. We also found that the more aggressive alveolar RMS cells express higher levels of c-MET than embryonal RMS cell lines and "home/seed" better into bone marrow after i.v. injection into immunocompromised **mice**. Because we could not find any activating mutations in the **kinase** region of c-MET or any evidence for HGF autocrine stimulation, we suggest that the increased response of RMS cell lines depends on overexpression of functional c-MET.

We conclude that HGF regulates the metastatic behavior of c-MET-positive RMS cells, directing them to the bone marrow and **lymph nodes**. Signaling from the c-MET receptor may also contribute to the resistance of RMS cells to conventional treatment modalities.

L13 ANSWER 10 OF 27 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-00219 BIOTECHDS
TITLE: Suppression of met expression: A possible cancer treatment; potential prostate cancer gene therapy involving use of ribozyme against receptor protein-tyrosine-**kinase**
AUTHOR: SHINOMIYA N; WOUDE GFV
CORPORATE SOURCE: Van Andel Res Inst
LOCATION: Shinomiya N, Van Andel Res Inst, Oncol Mol Lab, 333 Bostwick NE, Grand Rapids, MI 49503 USA
SOURCE: CLINICAL CANCER RESEARCH; (2003) 9, 14, 5085-5090
ISSN: 1078-0432
DOCUMENT TYPE: Journal
LANGUAGE: English
AB DERWENT ABSTRACT: Met is a receptor protein-tyrosine-**kinase** (EC-2.7.1.112) and the only known receptor for HGF/SF. This ligand/receptor signaling pair mediates a vast range of biological activities not only in normal organ development and physiological functions but also in tumor proliferation, progression, invasion, and metastasis. Tumor cells that express high levels of Met molecules on their surface are more malignant and metastatic. In many carcinomas, HGF/SF acting in a paracrine manner is produced by **stromal cells** adjacent to the tumor. Inhibition of Met expression suppresses the malignant progression of tumor cells. A ribozyme strategy has been used to suppress the growth of human glioblastorna tumors. Because overexpression of Met receptors is observed in a wide spectrum of carcinomas and considered to play a key role in the progression of cancer cells, targeting of this molecule could become one of the most useful treatment modalities for refractory cancers. Molecular targeting of the Met signaling pathways by using specifically designed genes. which target c-met, can be used as a treatment modality for controlling tumor growth and metastasis. An adeno virus vector expressing c-Met ribozyme inhibits tumorigenicity and **lymph node** metastasis of human prostate cancer cells by using an orthotopically implanted in vivo **mouse** model. In prostate cancer cells especially, high expression of Met is associated with resistance against chemotherapy including hormonal therapy and is often observed in the advanced stages of clinical cases. By reducing Met expression using a ribozyme that targets Met mRNA, tumor growth and **lymph node** metastasis were dramatically inhibited(6 pages)

L13 ANSWER 11 OF 27 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2003543598 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12881311
TITLE: Complexity within the plasma cell compartment of **mice** deficient in both E- and P-selectin: implications for plasma cell differentiation.
AUTHOR: Underhill Gregory H; Kolli K Pallav; Kansas Geoffrey S
CORPORATE SOURCE: Department of Microbiology-Immunology, Northwestern Medical School, 303 E Chicago Ave, Chicago, IL 60611, USA.
CONTRACT NUMBER: HL58710 (NHLBI)
SOURCE: Blood, (2003 Dec 1) 102 (12) 4076-83. Electronic Publication: 2003-07-24.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200401

ENTRY DATE: Entered STN: 20031119
Last Updated on STN: 20040115
Entered Medline: 20040114

AB Antibody-secreting plasma cells represent the critical end-stage effector cells of the humoral immune response. Here, we show that several distinct plasma cell subsets are concurrently present in the **lymph nodes**, spleen, and bone marrow of **mice** deficient in both E- and P-selectin. One of these subsets was a B220-negative immunoglobulin g (IgG) plasma cell population expressing low to negative surface levels of syndecan-1. Examination of the chemotactic responsiveness of IgG plasma cell subsets revealed that migration toward **stromal cell**-derived factor 1/CXC ligand 12 (SDF-1/CXCL12) was primarily limited to the B220-lo subset regardless of tissue source. Although B220-negative plasma cells did not migrate efficiently in response to CXCL12 or to other chemokines for which receptor mRNA was expressed, these cells expressed substantial surface CXC chemokine receptor-4 (CXCR4), and CXCL12 stimulation rapidly induced extracellular signal regulated **kinase** 1 (ERK1)/ERK2 phosphorylation, demonstrating that CXCR4 retained signaling capacity. Therefore, B220-negative plasma cells exhibit a selective uncoupling of chemokine receptor expression and signaling from migration. Taken together, our findings document the presence of significant heterogeneity within the plasma cell compartment, which suggests a complex step-wise scheme of plasma cell differentiation in which the degree of differentiation and tissue location can influence the chemotactic responsiveness of IgG plasma cells.

L13 ANSWER 12 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:153519 BIOSIS
DOCUMENT NUMBER: PREV200400148159
TITLE: Roles of PLC-beta2, -beta3, and PI3K in T-cell migration to SDF 1-alpha.
AUTHOR(S): Bach, Tami L. [Reprint Author]; Chen, Qing-Min [Reprint Author]; Jordan, Martha S.; Wu, Dianqing; Zigmond, Sally H.; Abrams, Charles S. [Reprint Author]
CORPORATE SOURCE: Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 768a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB Chemokines bind G-protein coupled receptors and play an essential role in both the immune and inflammatory responses. In T lymphocytes, little is known about the signaling pathways required for chemokine-mediated cell migration. Phospholipase C (PLC) and phosphatidylinositol 3-**kinase** (PI3K) are two distinct signaling molecules that have been proposed as potential candidates in the regulation of this process. Studies with knockout **mice** have demonstrated a critical role for D3-phosphoinositide production by PI3Kgamma in Galphai-coupled receptor-mediated neutrophil chemotaxis. Similar studies have failed to demonstrate a role for IP3 or DAG production by PLCbeta in this neutrophil response. In the current investigation, peripheral T-cells were isolated from the **lymph nodes** of wild type **mice** and **mice** with loss-of-function mutations of either PI3Kgamma, or both

of the two dominant lymphocyte PLCbeta isoforms (PLCbeta2 and PLCbeta3). Using a transwell assay, migration of lymphocytes toward SDF-1alpha (37.5 nM) was quantitated after 3 hours, the time point at which migration was maximal for both wild type and knockout T-cells. We found that lymphocytes isolated from wild type **mice** exhibited an eighteen-fold increase in migration with SDF-1alpha stimulation compared to baseline. In contrast, loss of either PLCbeta2beta3 or PI3Kgamma decreased chemokine-stimulated T-cell migration by 68%+-14% ($p<0.005$) and 12+-4% ($p<0.5$), respectively. The impaired sensitivity of the PLCbeta2/beta3-null T-cells occurred over a wide range of agonist, and in contrast to wild type lymphocytes, a large percentage of migration in the PLCbeta2/beta3-null T-cells was due to SDF-induced chemokinesis and not chemotaxis. Chelation of intracellular calcium by BAPTA (30 nM) decreased the chemotactic response of wild type lymphocytes, but pharmacologic inhibition of PKC isoforms by GF109203x (5 muM) or Go 6976 (5 muM) did not impair T-cell migration. Furthermore, SDF-1alpha-induced calcium efflux was not detected in the PLCbeta2beta3-null lymphocytes. This suggests that the T-cell migration defect seen in the PLCbeta2/beta3-null T-cells may be due to an impaired ability to increase intracellular calcium, while there appears to be little requirement for the stimulation of PKC. We have also found that inhibition of PI3K by either wortmannin (100 nM) or LY294002 (50 muM), decreased SDF-1alpha-induced migration of wild type cells to near baseline, suggesting that PI3K does contribute to T-cell migration, but the PI3Kgamma isoform contributes relatively little to this process. These results show that in vivo phospholipid second messengers generated by PLCbeta and isoforms of PI3K, other than PI3Kgamma, play a critical role in lymphocyte chemotaxis. Our data demonstrate that although PLCbeta-mediated signaling plays no role in neutrophil chemotaxis, it makes a substantial contribution to this process within T lymphocytes.

L13 ANSWER 13 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:451651 BIOSIS
DOCUMENT NUMBER: PREV200300451651
TITLE: Involvement of **stromal cell**-derived factor-1/CXCR4 signaling in **lymph node** metastasis of oral squamous cell carcinoma.
AUTHOR(S): Uchida, Daisuke [Reprint Author]; Begum, Nasima-Mila; Almofti, Ammar; Kawamata, Hitoshi; Nakashiro, Koh-Ichi; Tateishi, Yoshihisa; Hamakawa, Hiroyuki; Yoshida, Hideo; Sato, Mitsunobu
CORPORATE SOURCE: 2nd Dept. Oral and Maxillofacial Surgery, School of Dentistry, Tokushima University, Tokushima, Japan
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (July 2003) Vol. 44, pp. 452. print. Meeting Info.: 94th Annual Meeting of the American Association for Cancer Research. Washington, DC, USA. July 11-14, 2003. ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Oct 2003 Last Updated on STN: 1 Oct 2003

L13 ANSWER 14 OF 27 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 2003491192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14567988
TITLE: Possible role of **stromal-cell**-derived factor-1/CXCR4 signaling on **lymph node** metastasis of oral squamous cell carcinoma.
AUTHOR: Uchida Daisuke; Begum Nasima Mila; Almofti Ammar; Nakashiro

Koh-ichi; Kawamata Hitoshi; Tateishi Yoshihisa; Hamakawa Hiroyuki; Yoshida Hideo; Sato Mitsunobu

CORPORATE SOURCE: Second Department of Oral and Maxillofacial Surgery, Tokushima University School of Dentistry, 3-18-15 Kuramoto, Tokushima 770-8504, Japan.. daisuke@dent.tokushima-u.ac.jp

SOURCE: Experimental cell research, (2003 Nov 1) 290 (2) 289-302. Journal code: 0373226. ISSN: 0014-4827.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200312

ENTRY DATE: Entered STN: 20031022
Last Updated on STN: 20031219
Entered Medline: 20031202

AB We examined the role of chemokine signaling on the **lymph node** metastasis of oral squamous cell carcinoma (SCC) using **lymph node** metastatic (HNt and B88) and nonmetastatic oral SCC cells. Of 13 kinds of chemokine receptors examined, only CXCR4 expression was up-regulated in HNt and B88 cells. CXCR4 ligand, **stromal-cell**-derived factor-1alpha (SDF-1alpha; CXCL12), induced characteristic calcium fluxes and chemotaxis only in CXCR4-expressing cells. CXCR4 expression in metastatic cancer tissue was significantly higher than that in nonmetastatic cancer tissue or normal gingiva. Although SDF-1alpha was undetectable in either oral SCC or normal epithelial cells, submandibular **lymph nodes** expressed the SDF-1alpha protein, mainly in the **stromal cells**, but occasionally in metastatic cancer cells. The conditioned medium from lymphatic **stromal cells** promoted the chemotaxis of B88 cells, which was blocked by the CXCR4 neutralization. SDF-1alpha rapidly activated extracellular signal-regulated **kinase** (ERK)1/2 and Akt/protein **kinase** B (PKB), and their synthetic inhibitors attenuated the chemotaxis by SDF-1alpha. SDF-1alpha also activated Src family **kinases** (SFKs), and its inhibitor PP1 diminished the SDF-1alpha-induced chemotaxis and activation of both ERK1/2 and Akt/PKB. These results indicate that SDF-1/CXCR4 signaling may be involved in the establishment of **lymph node** metastasis in oral SCC via activation of both ERK1/2 and Akt/PKB induced by SFKs.

L13 ANSWER 15 OF 27 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:215250 SCISEARCH

THE GENUINE ARTICLE: 649WP

TITLE: Phase I dose escalation clinical trial of adenovirus vector carrying osteocalcin promoter-driven herpes simplex virus thymidine **kinase** in localized and metastatic hormone-refractory prostate cancer

AUTHOR: Kubo H; Gardner T A; Wada Y; Koeneman K S; Gotoh A; Yang L; Kao C H; Lim S D; Amin M B; Yang H; Black M E; Matsubara S; Nakagawa M; Gillenwater J Y; Zhau H Y E; Chung L W K (Reprint)

CORPORATE SOURCE: Emory Univ, Sch Med, Winship Canc Inst, Dept Urol, Mol Urol & Therapeut Program, 1365-B Clifton Rd, Room B5101, Atlanta, GA 30322 USA (Reprint); Emory Univ, Sch Med, Winship Canc Inst, Dept Urol, Mol Urol & Therapeut Program, Atlanta, GA 30322 USA; Indiana Univ, Med Ctr, Dept Urol, Indianapolis, IN 46202 USA; Kobe Univ, Sch Med, Dept Urol, Kobe, Hyogo 6500017, Japan; Univ Virginia Hlth Syst, Dept Urol, Charlottesville, VA 22908 USA; Emory Univ, Sch Med, Dept Pathol & Lab Med, Atlanta, GA 30322 USA; Washington State Univ, Dept Pharmaceut Sci, Pullman, WA 99164 USA; Kagoshima Univ, Fac Med, Dept Urol,

Kagoshima 8908506, Japan
COUNTRY OF AUTHOR: USA; Japan
SOURCE: HUMAN GENE THERAPY, (FEB 2003) Vol. 14, No. 3, pp. 227-241

Publisher: MARY ANN LIEBERT INC PUBL, 2 MADISON AVENUE, LARCHMONT, NY 10538 USA.
ISSN: 1043-0342.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 42

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Osteocalcin (OC), a major noncollagenous bone matrix protein, is expressed prevalently in prostate cancer epithelial cells, adjacent fibromuscular **stromal cells**, and osteoblasts in locally recurrent prostate cancer and prostate cancer bone metastasis [Matsubara, S., Wada, Y., Gardner, T. A., Egawa, M., Park, M. S., Hsieh, C. L., Zhau, H. E., Kao, C., Kamidono, S., Gillenwater, J.Y., and Chung, L. W. (2001). Cancer Res. 61, 6012-6019]. We constructed an adenovirus vector carrying osteocalcin promoter-driven herpes simplex virus thymidine **kinase** (Ad-OC-hsv-TK) to cotarget prostate cancer cells and their surrounding **stromal cells**. A phase I dose escalation clinical trial of the intralesional administration of Ad-OC-hsv-TK followed by oral valacyclovir was conducted at the University of Virginia (Charlottesville, VA) in 11 men with localized recurrent and metastatic hormone-refractory prostate cancer (2 local recurrent, 5 osseous metastasis, and 4 **lymph node** metastasis) in order to determine the usefulness of this vector for the palliation of androgen-independent prostate cancer metastasis. This is the first clinical trial in which therapeutic adenoviruses are injected directly into prostate cancer **lymph node** and bone metastasis. Results show that (1) all patients tolerated this therapy with no serious adverse events; (2) local cell death was observed in treated lesions in seven patients (63.6%) as assessed by TUNEL assay, and histomorphological change (mediation of fibrosis) was detected in all posttreated specimens; (3) one patient showed stabilization of the treated lesion for 317 days with no alternative therapy. Of the two patients who complained of tumor-associated symptoms before the treatment, one patient with bone pain had resolution of pain, although significant remission of treated lesions was not observed by image examination; (4) CD8-positive T cells were predominant compared with CD4-positive T cells, B cells (L26 positive), and natural killer cells (CD56 positive) in posttreated tissue specimens; (5) levels of HSV TK gene transduction correlated well with coxsackie-adenovirus receptor expression but less well with the titers of adenovirus injected; and (6) intrinsic OC expression and the efficiency of HSV TK gene transduction affected the levels of HSV TK protein expression in clinical specimens. Our data suggest that this form of gene therapy requires further development for the treatment of androgen-independent prostate cancer metastasis although histopathological and immunohistochemical evidence of apoptosis was observed in the specimens treated. Further studies including the development of viral delivery will enhance the efficacy of Ad-OC-hsv-TK.

L13 ANSWER 16 OF 27 MEDLINE on STN
ACCESSION NUMBER: 2003003088 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12393730
TITLE: CCR7-mediated physiological lymphocyte homing involves activation of a tyrosine **kinase** pathway.
AUTHOR: Stein Jens V; Soriano Silvia F; M'rini Christine; Nombela-Arrieta Cesar; de Buitrago Gonzalo Gonzalez; Rodriguez-Frade Jose Miguel; Mellado Mario; Girard Jean-Philippe; Martinez-A Carlos
CORPORATE SOURCE: Department of Immunology and Oncology, Centro Nacional de Biotecnologia/Consejo Superior de Investigaciones

Cientificas (CSIC), Madrid, Spain.. jstein@cnb.uam.es
SOURCE: Blood, (2003 Jan 1) 101 (1) 38-44. Electronic Publication: 2002-06-28.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030103
Last Updated on STN: 20030331
Entered Medline: 20030318

AB Homing of blood-borne lymphocytes to peripheral **lymph nodes** (PLNs) is a multistep process dependent on the sequential engagement of L-selectin, which mediates lymphocyte rolling along the luminal surface of high endothelial venules (HEVs), followed by activation of lymphocyte integrins and transmigration through HEVs. Within lymphoid tissue, B and T lymphocytes then migrate toward specific microenvironments such as B-cell follicles and the paracortex, respectively. The lymphocyte-expressed chemokine receptor CCR7 is playing an important role during this process, as its HEV-presented ligands CCL19 and CCL21 can trigger rapid integrin activation under flow in addition to inducing a chemotactic response, which may participate in transmigration and/or interstitial migration. Here, we report that Tyrphostin (Tyr) AG490, a pharmacological inhibitor of Janus family tyrosine **kinases** (Jaks), blocked the chemotactic response of primary **mouse** lymphocytes to CCL19 and CCL21 in a dose-dependent manner. Furthermore, Tyr AG490 inhibited rapid CCL21-mediated up-regulation of alpha4 and beta2 integrin adhesiveness in static adhesion assays and under physiological flow, whereas adhesion induced by phorbol myristate acetate remained unaltered. Using intravital microscopy of subiliac PLNs in **mice**, we found that adoptively transferred Tyr AG490-treated lymphocytes adhered significantly less in HEVs compared with control cells, although L-selectin-mediated rolling was similar in both samples. Finally, we observed rapid Jak2 phosphorylation in CCL21-stimulated primary **mouse** lymphocytes. Thus, our study suggests a role for Jak tyrosine **kinases** during CCR7-mediated lymphocyte recirculation.

L13 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:120036 HCAPLUS
DOCUMENT NUMBER: 138:236622
TITLE: RelB in secondary lymphoid organ development: differential regulation by lymphotoxin and tumor necrosis factor signaling pathways
AUTHOR(S): Yilmaz, Z. Buket
CORPORATE SOURCE: Institut fuer Toxikologie und Genetik, Germany
SOURCE: Wissenschaftliche Berichte - Forschungszentrum Karlsruhe (2002), FZKA 6793, i-xv, 1-117
CODEN: WBFKF5; ISSN: 0947-8620
DOCUMENT TYPE: Report
LANGUAGE: English

AB Primary lymphoid organs are the major sites of lymphopoiesis where lymphocytes proliferate and mature into functional but naive cells. Secondary lymphoid organs are sites where these lymphocytes encounter antigens and elicit immune responses. RelB is a member of the Rel/NF-κB family of inducible dimeric transcription factors. RelB is abundantly expressed in secondary lymphoid organs, such as spleen, **lymph nodes**, and Peyer's patches (PP). RelB-deficient **mice** have improper spleen structure and lack organizing centers for PPs, defects that can not be restored by the adoptive transfer of wild-type bone marrow cells. The work presented here revealed a reduction in expression of the homing chemokines B lymphocyte chemoattractant (BLC) and

secondary lymphoid organ chemokine (SLC) in RelB-deficient spleen, suggesting a role for RelB in proper expression of chemokines by splenic **stromal cells**. Moreover, interleukin-7 (IL-7)-induced expression of lymphotoxin (LT) in intestinal cells, a crucial step in early PP development, was not impaired in RelB-deficient embryos, suggesting functional hematopoietic inducers and a defect in LTβ receptor (LTβR) expressing stromal responders. Activation of LTβR signaling in fibroblasts resulted in the specific induction of p52-RelB heterodimers, while tumor necrosis factor (TNF) induced classical p50-RelA NF-κB complexes. LTβR-induced RelB nuclear translocation and DNA binding of p52-RelB heterodimers required the degradation of the inhibitory p52 precursor, p100, which was dependent on the IκB **kinase** (IKK) complex subunit IKKα, but not on IKKβ or IKKγ. In contrast to LTβR signaling, TNFR signaling increased p100 and RelB levels both in cytoplasm and nucleus and RelB was bound to p100 in both compartments. Despite the abundant presence of RelB in the nucleus, RelB DNA binding was almost undetectable in TNF treated fibroblasts. Forced expression of p50 and p52 could not rescue the lack of DNA binding. In contrast, RelB DNA binding increased in cells lacking the C-terminus of p100, but not of p105, strongly suggesting that it is the specific inhibitory function of the C-terminal domain of p100, rather than the lack of the heterodimerization partner, which prevents RelB DNA binding in TNF-stimulated fibroblasts. Thus, RelB and p52 in **stromal cells** could function in the proper development of the spleen by regulating the expression of chemokines such as BLC. Furthermore, generation of p52-RelB heterodimers by the LTβR pathway involving p100 degradation, appears to be a critical step in the formation of PP anlage.

REFERENCE COUNT: 118 THERE ARE 118 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 18 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:164949 BIOSIS
DOCUMENT NUMBER: PREV200300164949
TITLE: VEGFR-3 in Cornea Lymphangiogenesis and APC Trafficking.
AUTHOR(S): Chen, L. [Reprint Author]; Hamrah, P. [Reprint Author]; Zhang, Q. [Reprint Author]; Dana, M. R. [Reprint Author]
CORPORATE SOURCE: Department of Ophthalmology, Schepens Eye Research Institute, Harvard Medical School, Boston, MA, USA
SOURCE: ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002, pp. Abstract No. 2268. cd-rom. Meeting Info.: Annual Meeting of the Association For Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. May 05-10, 2002.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Apr 2003
Last Updated on STN: 2 Apr 2003

AB Purpose: Previous data from this lab indicate that lymphatic flow from the cornea to draining **lymph nodes** (LN) plays an important role in corneal immunity. Specifically, corneal transplantation to BALB/c hosts that had their cervical LN excised before surgery showed indefinitely and universal graft acceptance (Yamagami S. & Dana M.R., 2001). VEGFR-3 (Flt-4) is a receptor tyrosine **kinase** which is mainly expressed on the lymphatic endothelium in adult tissues. The purpose of this study is to elucidate the expressional changes of VEGFR-3 during corneal neovascularization (NV) and its possible roles in cornea lymphangiogenesis and APC trafficking. Methods: Corneal NV was induced by intrastromal 11-0 nylon sutures in Balb/c **mice**. Eyes were

procured 1, 3, 7, 14 days after the manipulation. Lymphatic vessels and VEGFR-3 positive cells were identified by confocal microscopy with immunofluorescence staining. Results: Cornea lymphatic vessels were detected with VEGFR-3 and CD31 double staining in corneal whole mounts starting at day 3 during induction of corneal NV. Cross sectional studies additionally revealed that the ocular surface epithelium of normal eyes express high levels of VEGFR-3. A sharp increase in VEGFR-3 staining in the corneal stroma was observed during the first week after induction of NV and a transient increase of VEGFR-3 expression on the epithelial layers of the limbus and conjunctival region around day 3 was also found. Additionally, corneal inflammation was associated with enhanced expression of VEGFR-3 by CD11c+ corneal dendritic cells. Conclusion: The expression of VEGFR-3 in the cornea and ocular surface is modified during corneal NV, both at the level of lymphatic vessels, and epithelial and **stromal cells**. These changes may affect trafficking of antigens and/or antigen-presenting cells from the eye to lymphoid organs and provide one explanation for why eyes with NV are considered 'high-risk' candidates for allograft survival. Additional studies including the use of recombinant VEGFR-3 chimeric protein in allograft cornea transplantation were undertaken to further define the possible functional roles of this receptor in lymphatic drainage and graft survival. Support: NIH/NEI Grant EY12963.

L13 ANSWER 19 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:356767 BIOSIS
DOCUMENT NUMBER: PREV200300356767
TITLE: Loss of Function Mutations of PI3Kgamma or PLCbeta2/beta3 Impair T-Cell Migration to SDF.
AUTHOR(S): Bach, Tami L. [Reprint Author]; Huang, Minzhou [Reprint Author]; Wu, Dianqing [Reprint Author]; Zigmond, Sally H. [Reprint Author]; Abrams, Charles S. [Reprint Author]
CORPORATE SOURCE: Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA, USA
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2633. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 18 Sep 2003

AB Leukocyte chemotaxis plays a role in both the immune and inflammatory response. **Stromal cell**-derived factor-1alpha (SDF-1alpha) is a member of the CXC chemokine subfamily that stimulates T lymphocytes via activation of a Galphai-coupled receptor. Studies with knockout **mice** have demonstrated a critical role for D3-phosphoinositide production by phosphatidylinositol 3-**kinase** gamma (PI3Kgamma) in Galphai-coupled receptor mediated neutrophil chemotaxis. Similar studies have failed to demonstrate a role for IP3 or DAG production by phospholipase Cbeta (PLCbeta) in this neutrophil response. The role of phospholipid second messengers generated by PI3Kgamma or PLCbeta in lymphocyte chemotaxis is less well known. In the current investigation, **murine** T lymphocytes were studied to determine whether loss of function mutations within either PI3Kgamma, or both of the two dominant lymphocyte PLCbeta isoforms (PLCbeta2 & PLCbeta3), affected lymphocyte migration in response to SDF-1alpha. Using a transwell assay, peripheral T-cells were isolated from the **lymph nodes** of knockout and control **mice**. Migration from the

top chamber into the bottom chamber after 3 hours was quantitated in the absence, or presence, of 37.5 nM SDF-1alpha in the lower chamber. Flow cytometry was used to quantitate the number of cells in each chamber. The lymphocytes isolated from control wild type **mice** exhibited a 2.5-4-fold increase in migration with SDF-1alpha stimulation compared to baseline. In contrast, loss of either PI3Kgamma or PLC beta2/beta3 decreased chemokine-stimulated cell migration by 29.0% +/- 5.5% ($p<0.05$) and 49.3% +/- 3.1% ($p<0.001$), respectively. Furthermore, inhibition of PI3K by either wortmannin (233 nM) or LY294002 (50 muM), completely eliminated SDF-1alpha-induced migration of either the wild type cells or cells lacking PI3Kgamma. This latter observation suggests that PI3K isoforms other than PI3Kgamma, also contribute to the chemotactic response. These results show that in vivo phospholipid second messenger formation by both PI3Kgamma and PLCbeta plays a critical role in lymphocyte chemotaxis. Our data demonstrate that although PLCbeta-mediated signaling plays no role in neutrophil chemotaxis, it makes a substantial contribution to this process within T-lymphocytes.

L13 ANSWER 20 OF 27 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 2001357671 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11418238
TITLE: Identification of a new fibroblast growth factor receptor, FGFR5.
AUTHOR: Sleeman M; Fraser J; McDonald M; Yuan S; White D; Grandison P; Kumble K; Watson J D; Murison J G
CORPORATE SOURCE: Genesis Research and Development Corporation Ltd., 1 Fox Street, Parnell, Auckland, New Zealand.
SOURCE: Gene, (2001 Jun 27) 271 (2) 171-82.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF321300; GENBANK-AF321301
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010827
Last Updated on STN: 20010827
Entered Medline: 20010823

AB A novel fibroblast growth factor receptor (FGFR), designated FGFR5, was identified from an EST database of a **murine lymph node stromal cell** cDNA library. The EST has approximately 32% identity to the extracellular domain of FGFR1-4. Library screening with this EST identified two full-length alternative transcripts which we designated as FGFR5 beta and FGFR5 gamma. The main difference between these transcripts is that FGFR5 beta contains three extracellular Ig domains whereas FGFR5 gamma contains only two. A unique feature of FGFR5 is that it does not contain an intracellular tyrosine **kinase** domain. Predictive structural modelling of the extracellular domain of FGFR5 gamma suggested that it was a member of the I-set subgroup of the Ig-superfamily, consistent with the known FGFRs. Northern analysis of **mouse** and human FGFR5 showed detectable mRNA in a broad range of tissues, including kidney, brain and lung. Genomic sequencing identified four introns but identified no alternative transcripts containing a tyrosine **kinase** domain. Extracellular regions of FGFR5 beta and 5 gamma were cloned in-frame with the Fc fragment of human IgG(1) to generate recombinant non-membrane bound protein. Recombinant FGFR5 beta Fc and R5 gamma Fc demonstrated specific binding to the ligand FGF-2, but not FGF-7 or EGF. However, biological data suggest that FGF-2 binding to these proteins is with lower affinity than its cognate receptor FGFR2C. The above data indicate that this receptor should be considered as the fifth member of the FGFR family.

L13 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:861815 HCAPLUS
DOCUMENT NUMBER: 134:26116
TITLE: Protein and cDNA sequences of human and **mouse** protein **kinase** sequence homologs, and uses thereof in identifying novel **kinase** inhibitor
INVENTOR(S): Bird, Timothy A.; Virca, G. Duke; Martin, Unja; Anderson, Dirk M.
PATENT ASSIGNEE(S): Immunex Corporation, USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073468	A1	20001207	WO 2000-US14696	20000526
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2374612	AA	20001207	CA 2000-2374612	20000526
EP 1181374	A1	20020227	EP 2000-939378	20000526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6514719	B1	20030204	US 2000-579664	20000526
US 2003162277	A1	20030828	US 2003-355975	20030130
US 6759223	B2	20040706		

PRIORITY APPLN. INFO.:

US 1999-136781P	P	19990528
US 2000-579664	A3	20000526
WO 2000-US14696	W	20000526

AB The invention is directed to purified and isolated novel **murine** and human **kinase** polypeptides, the nucleic acids encoding such polypeptides, processes for production of recombinant forms of such polypeptides, antibodies generated against these polypeptides, fragmented peptides derived from these polypeptides, and the uses of the above. Protein and cDNA sequences of novel human **mouse** protein **kinase** sequence homologs are identified by querying sequence data bases with DNA sequences from **murine** dendritic cell, **murine lymph node stromal cell**, human dendritic cell and human spleen cDNA library, using an algorithm designed to recognize **kinase** subdomains. The invention further relates to methods for identifying novel **kinase** inhibitor.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 22 OF 27 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 1999113739 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9916701
TITLE: Galectin-1 specifically modulates TCR signals to enhance TCR apoptosis but inhibit IL-2 production and proliferation.
AUTHOR: Vespa G N; Lewis L A; Kozak K R; Moran M; Nguyen J T; Baum L G; Miceli M C
CORPORATE SOURCE: Department of Microbiology and Immunology, University of

California, Los Angeles, School of Medicine, 90095, USA.
CONTRACT NUMBER: CA-16042 (NCI)
R29 CA65979-01 (NCI)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1999 Jan 15) 162 (2) 799-806.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990223
Last Updated on STN: 19990223
Entered Medline: 19990208

AB Galectin-1 is an endogenous lectin expressed by thymic and **lymph node stromal cells** at sites of Ag presentation and T cell death during normal development. It is known to have immunomodulatory activity in vivo and can induce apoptosis in thymocytes and activated T cells (1-3). Here we demonstrate that galectin-1 stimulation cooperates with TCR engagement to induce apoptosis, but antagonizes TCR-induced IL-2 production and proliferation in a **murine** T cell hybridoma and freshly isolated **mouse** thymocytes, respectively. Although CD4+ CD8+ double positive cells are the primary thymic subpopulation susceptible to galectin-1 treatment alone, concomitant CD3 engagement and galectin-1 stimulation broaden susceptible thymocyte subpopulations to include a subset of each CD4- CD8-, CD4+ CD8+, CD4- CD8+, and CD4+ CD8- subpopulations. Furthermore, CD3 engagement cooperates with suboptimal galectin-1 stimulation to enhance cell death in the CD4+ CD8+ subpopulation. Galectin-1 stimulation is shown to synergize with TCR engagement to dramatically and specifically enhance extracellular signal-regulated **kinase**-2 (ERK-2) activation, though it does not uniformly enhance TCR-induced tyrosine phosphorylation. Unlike TCR-induced IL-2 production, TCR/galectin-1-induced apoptosis is not modulated by the expression of **kinase** inactive or constitutively activated Lck. These data support a role for galectin-1 as a potent modulator of TCR signals and functions and indicate that individual TCR-induced signals can be independently modulated to specifically affect distinct TCR functions.

L13 ANSWER 23 OF 27 EMBASE
on STN
ACCESSION NUMBER: 1998113479 EMBASE
TITLE: Characteristics of the conditioned medium produced by CA-12 **lymph node stromal cells**.
AUTHOR: Lee S.-H.; Lee D.-S.; Seu Y.-B.; Kim J.-G.; Tsuruo T.; Hong S.-D.
CORPORATE SOURCE: S.-D. Hong, Department of Microbiology, Kyungpook National University, Taegu 702-701, Korea, Republic of.
leesh@rockvex.rockefeller.edu
SOURCE: Journal of Microbiology and Biotechnology, (1998) Vol. 8, No. 1, pp. 74-80.
Refs: 21
ISSN: 1017-7825 CODEN: JOMBES
COUNTRY: Korea, Republic of
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19980520

Last Updated on STN: 19980520

AB CS-21 lymphoma cells that preferentially metastasize to **lymph nodes** after s.c. inoculation into BALB/c **mice** were grown in vitro in the presence of CA-12 **stromal cells** isolated from **lymph nodes**. In order to obtain fundamental data on the identification and characterization of the soluble factors produced by CA-12 **stromal cells**, the conditioned medium of CA-12 **stromal cells** that inhibited apoptosis of CS-21 cells was examined. Various analytical treatments revealed that the soluble factors in CA-12 conditioned medium are very sensitive to heat treatment and trypsinization. Moreover CA- 12 conditioned medium has an affinity with heparin but not with Con-A. In addition to these, the activity of CA-12 conditioned medium was blocked by H- 7, a PKC inhibitor, but the conditioned medium could not induce the differentiation of thymocytes. We concluded that CA-12 conditioned medium contains **stromal cell**-derived apoptosis-inhibitory molecules that play an important role in proliferation of CS-21 cells by suppressing cell apoptosis.

L13 ANSWER 24 OF 27 MEDLINE on STN
ACCESSION NUMBER: 97122514 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8968108
TITLE: Induction of fibroblast gelatinase B expression by direct contact with cell lines derived from primary tumor but not from metastases.
AUTHOR: Segain J P; Harb J; Gregoire M; Meflah K; Menanteau J
CORPORATE SOURCE: Unite Institut National de la Sante et de la Recherche Medicale U 419,Institut de Biologie, Centre Hospitalier Universitaire, Nantes, France.
SOURCE: Cancer research, (1996 Dec 1) 56 (23) 5506-12. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 20000303
Entered Medline: 19970124

AB During cancer progression, tumor cells interact with **stromal cells**. As a consequence, matrix metalloproteinases are produced that contribute to the degradation of the extracellular matrix. This study used coculture systems to investigate fibroblast interaction with three colon cancer cell lines isolated from a single patient. Cells from primary colorectal carcinoma, but not from corresponding liver or **lymph node** metastases, induced gelatinase B expression by fibroblasts of different tissue origin. Remarkably, direct cell-cell contact was required for this induction, which occurred at the pretranslational level (as revealed by Northern blot analysis) and was completely blocked by anti-beta1 integrin monoclonal antibody, but only partially blocked by anti-alpha5 or anti-alpha(v). Induction was also inhibited by cytochalasin D, staurosporine, or dexamethasone, suggesting the need, respectively, for an organized actin cytoskeleton, protein **kinase** C, and AP-1-driven gene transcription. Our data suggest that direct tumor-**stromal cell** contact is one inductive event involved in matrix metalloproteinase expression by **stromal cells**.

L13 ANSWER 25 OF 27 EMBASE on STN DUPLICATE 8
ACCESSION NUMBER: 95155187 EMBASE
DOCUMENT NUMBER: 1995155187
TITLE: Involvement of CD45 in adhesion and suppression of

apoptosis of **mouse** malignant T-lymphoma cells.
AUTHOR: Hanaoka K.; Fujita N.; Lee S.-H.; Seimiya H.; Naito M.; Tsuruo T.
CORPORATE SOURCE: Laboratory of Biomedical Research, Molecular/Cellular Biosciences Inst., University of Tokyo, 1-1-1, Yayoi,Bunkyo-ku, Tokyo 113, United States
SOURCE: Cancer Research, (1995) Vol. 55, No. 10, pp. 2186-2190. ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 950612
Last Updated on STN: 950612

AB **Mouse** malignant T-lymphoma CS-21 cells undergo apoptotic cell death in vitro in the absence of **lymph node stromal cells** but escape apoptosis and proliferate when they are attached to CA-12 **stromal cells**. A monoclonal antibody raised against CS-21 cell surface molecules (MCS-5) recognized a M(r) 168,000 protein, inhibited binding of CS-21 cells to CA-12 **stromal cells**, and suppressed apoptosis in CS-21 cells. To identify the M(r) 168,000 protein, we purified it with MCS-5 affinity chromatography and ion exchange chromatography. Partial amino acid sequences of the purified M(r) 168,000 protein were identical to those of CD45, a transmembrane tyrosine phosphatase. The purified protein possessed tyrosine phosphatase activity and was recognized by an anti-CD45 monoclonal antibody. The M(r) 168,000 protein was identified as CD45. To determine the CD45 isoform, we cloned the CD45 gene from the cDNA library of CS-21. Sixteen or 18 clones encoded CD45RO (CD45 lacking exons 4, 5, and 6), and the remainder lacked exons 4, 5, 6, and 7. Like MCS-5, an anti-CD45 monoclonal antibody, also inhibited binding of CS-21 cells to CA-12 cells and suppressed apoptosis in CS-21 cells. Our present results indicate that CD45RO expressed un CS-21 cells mediates adhesion to CA-12 cells and suppression of apoptosis.

L13 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:491699 HCAPLUS
DOCUMENT NUMBER: 122:236647
TITLE: Apoptosis inhibition by anti-Mr 23,000 (Thy-1) monoclonal antibodies without inducing bcl-2 expression
AUTHOR(S): Fujita, Naoya; Naito, Mikihiko; Lee, Sang-Han; Hanaoka, Kenji; Tsuruo, Takashi
CORPORATE SOURCE: Inst. Molecular Cellular Biosciences, Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Cell Growth & Differentiation (1995), 6(4), 355-62 CODEN: CGDIE7; ISSN: 1044-9523
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Mouse** malignant T-lymphoma CS-21 cells grow in vitro in the presence of CA-12 **stromal cells**, but they undergo apoptotic cell death with DNA fragmentation when cultured alone. Because apoptosis of CS-21 cells was not inhibited by soluble factors secreted from CA-12 **stromal cells**, cell-cell interactions between the two seemed to be important to inhibit apoptosis. The authors found that CS-21 cell adhesion was mediated by Mr 168,000 and Mr 23,000 proteins and that apoptosis-inhibitory signals were transmitted through these proteins. In this study, the authors identified the Mr 23,000 cell adhesion mol. as a glycosylphosphatidylinositol-anchored Thy-1 (CD90) glycoprotein. Crosslinking of Mr 23,000 protein with anti-Mr 23,000 mAb

and a second antibody transiently raised the [Ca2+]i and activated calcineurin in CS-21 cells, as has been observed in normal T lymphocytes stimulated by crosslinking anti-Thy-1 mAbs. However, differing from normal T lymphocytes, CS-21 cells could grow either by the transient increase in [Ca2+]i or by the activation of protein **kinase** C. Furthermore, Mr 23,000 protein-mediated cell survival of CS-21 cells was not accompanied by expression of the apoptosis-inhibiting protein bcl-2, although protein **kinase** C-activated cell survival was attended by bcl-2 expression. These results indicate that the Mr 23,000 protein (Thy-1) of CS 21 lymphoma cells functions as a cell adhesion mol. capable of transducing signals of cell survival and growth that are not followed by bcl-2 expression.

L13 ANSWER 27 OF 27 MEDLINE on STN
ACCESSION NUMBER: 95331136 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7607087
TITLE: Developmental expression of the **mouse** c-rel proto-oncogene in hematopoietic organs.
AUTHOR: Carrasco D; Weih F; Bravo R
CORPORATE SOURCE: Department of Molecular Biology, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, New Jersey 08543-4000, USA.
SOURCE: Development (Cambridge, England), (1994 Oct) 120 (10) 2991-3004.
Journal code: 8701744. ISSN: 0950-1991.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950828
Last Updated on STN: 20000303
Entered Medline: 19950814

AB We have studied the expression of the c-rel proto-oncogene during **mouse** embryonic development and adult animals using in situ hybridization and immunocytochemical analysis. c-rel transcripts were detected late in development with an expression pattern that parallels the emergence and diversification of hematopoietic cells. In the embryo, c-rel is expressed first in the mesoderm-derived hematopoietic cells of the liver and later also in other hematopoietic tissues such as thymus and spleen. This correlation between c-rel expression and places of hematopoietic infiltration is conserved in the postnatal period, with expression of c-rel mRNA in the medullary region of the thymus and in splenic B cell areas, including the marginal zone and the outer region of the periarterial sheath. High levels of c-rel transcripts were also detected in the splenic germinal centers, **lymph nodes** and Peyer's patches. Using double immunofluorescence and cell preparations from different embryonic and adult hematopoietic organs, we have defined the pattern and cell types of c-rel expression in different hematopoietic cell lineages and in the **stromal cell** content of the thymus. By using electrophoretic mobility shift assays, we have also correlated c-Rel expression in spleen with kappa B-binding activity in the form of c-Rel/p50 and c-Rel/p52 heterodimers. The timing and pattern of expression of the c-rel proto-oncogene in the different cell lineages suggest that temporally regulated changes in c-Rel expression may be required for vertebrate hematopoiesis.

=> d his

(FILE 'HOME' ENTERED AT 12:14:19 ON 10 JUN 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,

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     LIFESCI' ENTERED AT 12:14:46 ON 10 JUN 2005
L1       1324738 S KINASE?
L2        395747 S LYMPH(A)NODE
L3         68040 S STROMAL(W)CELL
L4          5495 S L1 AND L2
L5           102 S L3 AND L4
L6       7110172 S CLON? OR EXPRESS? OR RECOMBINANT
L7            95 S L5 AND L6
L8            50 DUP REM L7 (45 DUPLICATES REMOVED)
L9       3990560 S MURINE OR MOUSE
L10            0 S L2(A)L3(A)L1
L11         1624 S L4 AND L9
L12           53 S L3 AND L11
L13           27 DUP REM L12 (26 DUPLICATES REMOVED)

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E1          307      BIRD T/AU
E2            1      BIRD T */AU
E3          197 --> BIRD T A/AU
E4            5      BIRD T B/AU
E5            2      BIRD T C/AU
E6          909      BIRD T D/AU
E7           21      BIRD T E/AU
E8           68      BIRD T G/AU
E9           42      BIRD T G C/AU
E10           3      BIRD T GEOFFREY/AU
E11          13      BIRD T GEOFFREY C/AU
E12           1      BIRD T GOEFFREY C/AU

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L14         197 "BIRD T A"/AU

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E3          131 --> VIRCA G D/AU
E4           47      VIRCA G DUKE/AU
E5            1      VIRCA GEORGE D/AU
E6            1      VIRCA GEORGE DUKE/AU
E7            1      VIRCAR A V/AU
E8            7      VIRCAVA D/AU
E9            1      VIRCAVA D K/AU
E10           2      VIRCAVA DAINA/AU
E11           7      VIRCAVA L/AU
E12          30      VIRCAVS M/AU

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L15         131 "VIRCA G D"/AU

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E2            1      ANDERSON D LONNIE/AU
E3         1948 --> ANDERSON D M/AU
E4            3      ANDERSON D M */AU
E5            1      ANDERSON D M A/AU
E6            1      ANDERSON D M JR/AU
E7            1      ANDERSON D M N/AU
E8          399      ANDERSON D M W/AU
E9            3      ANDERSON D MICHAEL/AU
E10         349      ANDERSON D N/AU
E11           1      ANDERSON D N E/AU
E12           1      ANDERSON D N W/AU
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L16        1948 "ANDERSON D M"/AU

=> d his

     (FILE 'HOME' ENTERED AT 12:14:19 ON 10 JUN 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:14:46 ON 10 JUN 2005
L1      1324738 S KINASE?
L2       395747 S LYMPH(A)NODE
L3        68040 S STROMAL(W)CELL
L4         5495 S L1 AND L2
L5          102 S L3 AND L4
L6      7110172 S CLON? OR EXPRESS? OR RECOMBINANT
L7           95 S L5 AND L6
L8           50 DUP REM L7 (45 DUPLICATES REMOVED)
L9      3990560 S MURINE OR MOUSE
L10           0 S L2(A)L3(A)L1
L11        1624 S L4 AND L9
L12          53 S L3 AND L11
L13          27 DUP REM L12 (26 DUPLICATES REMOVED)
                E BIRD T A/AU
L14         197 S E3
                E VIRCA G D/AU
L15         131 S E3
                E ANDERSON D M/AU
L16        1948 S E3

=> s l13 or l14 or l15 or l16
L17        2268 L13 OR L14 OR L15 OR L16

=> s l5 and l17
L18          27 L5 AND L17

=> dup rem l18
ENTER L# LIST OR (END):end

=> dup rem l18
PROCESSING COMPLETED FOR L18
L19          27 DUP REM L18 (0 DUPLICATES REMOVED)

=> d 1-17 ibib ab

L19  ANSWER 1 OF 27  SCISEARCH  COPYRIGHT (c) 2005 The Thomson Corporation  on
     STN
ACCESSION NUMBER:    2005:252300  SCISEARCH
THE GENUINE ARTICLE: 898JM
TITLE:               Two distinctive pathways for recruitment of naive and
                     primed IgM(+) B cells to the gut lamina propria
AUTHOR:              Suzuki K; Meek B; Doi Y; Honjo T; Fagarasan S (Reprint)
CORPORATE SOURCE:    RIKEN Res Ctr Allergy & Immunol, Tsurumi Ku, Kanagawa
                     2300045, Japan (Reprint); Kyoto Univ, Grad Sch Med, Dept
                     Med Chem, Sakyo Ku, Kyoto 6068501, Japan
COUNTRY OF AUTHOR:   Japan
SOURCE:              PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE
                     UNITED STATES OF AMERICA, (15 FEB 2005) Vol. 102, No. 7,
                     pp. 2482-2486.
                     Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW,
                     WASHINGTON, DC 20418 USA.
                     ISSN: 0027-8424.
DOCUMENT TYPE:       Article; Journal
LANGUAGE:            English
```

REFERENCE COUNT: 31

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Intestinal IgA(+) B cells are generated from IgM(+) B cells by in situ class switching in two separate gut microenvironments: organized follicular structures and lamina propria (LP). However, the origin of IgM(+) B cells in the gut LP is unknown. Transfer experiments to reconstitute IgM(+) B cells and IgA plasma cells in LP of aly/aly **mice**, which are defective in all organized follicular structures because of an NF-kappaB-inducing **kinase** (NIK) mutation, revealed that naive B cells can directly migrate to the LP. This migration requires NIK-dependent activation of gut **stromal cells**. By contrast, the entry of gut-primed IgM(+) B cells to the LIP is independent of **stromal cells** with functional NIK. Our results indicate that naive B cells directly migrate to the LIP by a distinct pathway from gut-primed B cells.

L19 ANSWER 2 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2005223785 EMBASE

TITLE: The role of CXCR4 in lung cancer metastasis and its possible mechanism.

AUTHOR: Su L.-P.; Zhang J.-P.; Xu H.-B.; Chen J.; Wang Y.; Xiong S.-D.

CORPORATE SOURCE: S.-D. Xiong, Department of Immunology, Shanghai Medical College of Fudan University, Shanghai 20032, China

SOURCE: National Medical Journal of China, (11 May 2005) Vol. 85, No. 17, pp. 1190-1194.
Refs: 16
ISSN: 0376-2491

COUNTRY: China

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
022 Human Genetics
029 Clinical Biochemistry

LANGUAGE: Chinese

SUMMARY LANGUAGE: Chinese; English

ENTRY DATE: Entered STN: 20050602
Last Updated on STN: 20050602

AB Objective: To investigate the role of CXCR4 in the metastasis of human lung cancer and its possible mechanism. Methods: Lung cancer cells of the lines 95C and 95D with high or low metastatic potential were transfeted with CXCR4 antisense plasmid pcDNA-ASX4, whole length eukaryotic expression plasmid pcDNA-CXCR4 (95D-ASX4 and 95C-X4 cell lines), and corresponding plasmid pcDNA3 (95C-pC and 95D-pC cell lines). 95C, 95C-pC, 95C-X4, 95D, and 95D-pC cells were injected subcutaneously into Balb/c nu/nu **mice**, 4 - 5 **mice** in a group. The **mice** were observed twice a week. Ten weeks later the **mice** were killed and the tumor in situ and the lungs were taken out to undergo histological examination. The effect of CXCR4 expression on the cell migration, MMP-2 activity, adhesion and GRO-a expression of lung cancer cells were detected by chemotaxis and chemoinvasion assay, zymography, adhesion assay and RT-PCR respectively. The polymerization of F-actin was measured by FACS and confocal microcopy. Western blotting was used to detect the phospharylation of ERK1/2 in 85D cells Results: Metastasis was not found in the **mice** injected with 95C and 95C-pC cells, and was seen in 2/5 of the **mice** injected with 95C-X4 cells, 3/4 of the **mice** injected with 95D and 95D-pC cells, 2/5 of the **mice** injected with 95D-ASX4 cells, however, the number of metastatic nodes in the lungs of 95D-ASX4 group was significantly less than those in the 95D and 95D-pC groups ($P = 0.044$). SDF-1a, a CXCR4 specific ligand, induced the migratory response and F-actin polymerization

in the lung cancer cells; SDF-1a promoted the MMP-2 activity, the adhesion to vascular endothelial cells and GRO-a expression; and neutralizing CXCR4 antibody inhibited these effects to some degree. Moreover, SDF-1a induced the phosphorylation of ERK1/2 in human lung cancer cells. Conclusion: Metastasis of human lung cancer depends on, to some degree, the interaction of CXCR4 and SDF-1 that are involved in this process by regulating the active locomotion, MMP-2 activity, adhesion ability or GRO-a expression.

L19 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:371064 HCAPLUS
DOCUMENT NUMBER: 140:373461
TITLE: Evaluation of breast cancer states and outcomes using gene expression profiles
INVENTOR(S): West, Mike; Nevins, Joseph R.; Huang, Andrew
PATENT ASSIGNEE(S): Synpac, Inc., USA; Duke Univerisity
SOURCE: PCT Int. Appl., 799 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004037996	A2	20040506	WO 2003-US33656		20031024
WO 2004037996	A3	20041229			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004083084	A1	20040429	US 2002-291878		20021112
WO 2004044839	A2	20040527	WO 2002-US38216		20021112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004106113	A1	20040603	US 2002-291886		20021112
PRIORITY APPLN. INFO.:			US 2002-420729P	P	20021024
			US 2002-421062P	P	20021025
			US 2002-421102P	P	20021025
			US 2002-424701P	P	20021108
			US 2002-424715P	P	20021108
			US 2002-424718P	P	20021108
			US 2002-291878	A	20021112
			US 2002-291886	A	20021112
			US 2002-425256P	P	20021112
			WO 2002-US38216	A	20021112
			WO 2002-US38222	A	20021112
			US 2003-448461P	P	20030221
			US 2003-448462P	P	20030221

US 2003-457877P P 20030327
US 2003-458373P P 20030331

AB The present invention relates generally to a method for evaluating and/or predicting breast cancer states and outcomes by measuring gene and metagene expression levels and integrating such data with clin. risk factors. Genes and metagenes whose expressions are correlated with a particular breast cancer risk factor or phenotype are provided using binary prediction tree modeling. The invention provides 175 genes associated with metagene predictors of **lymph node** metastasis, 216 genes associated with metagene predictors of breast cancer recurrence, and 496 metagenes related to breast cancer study. Methods of using the subject genes and metagenes in diagnosis and treatment methods, as well as drug screening methods, etc are also provided. In addition, reagents, media and kits that find use in practicing the subject methods are also provided.

L19 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:308529 HCAPLUS
DOCUMENT NUMBER: 140:333599
TITLE: Gene expression profile of human and **mouse** genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening
INVENTOR(S): Itoh, Mikito; Ogawa, Kaoru; Shinagawa, Akira; Sudo, Hajime; Ogawa, Hideoki; Ra, Chisei; Mitsuishi, Kouichi
PATENT ASSIGNEE(S): Genox Research, Inc., Japan; Juntendo University
SOURCE: PCT Int. Appl., 611 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004031386	A1	20040415	WO 2003-JP9808	20030801

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-229318 A 20020806
JP 2003-136543 A 20030514

AB This invention provides gene expression profile between a rash site and a no-rash site in a patient with atopic dermatitis or a patient with psoriasis. The invention also provides gene expression profile between a no-rash site in such a disease and a normal subject. Animal models, particularly **mouse** for those diseases are also claimed. The gene expression profile provided in this invention can be used for diagnosis, therapy, and drug screening for atopic dermatitis and psoriasis.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 27 MEDLINE on STN
ACCESSION NUMBER: 2004627248 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15585839
TITLE: Intestinal cryptopatch formation in **mice** requires

lymphotoxin alpha and the lymphotoxin beta receptor.
AUTHOR: Taylor Rebekah T; Lugering Andreas; Newell Kenneth A; Williams Ifor R
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, GA 30322, USA.
CONTRACT NUMBER: DK64399 (NIDDK)
DK64730 (NIDDK)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2004 Dec 15) 173 (12) 7183-9.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20041220
Last Updated on STN: 20050209
Entered Medline: 20050208

AB Interactions between lymphotoxin (LT)alpha(1)beta(2) on inducer cells and the lymphotoxin beta receptor (LTbetaR) on **stromal cells** initiate development of **lymph nodes** and Peyer's patches. In this study, we assessed the contributions of LTalpha and LTbetaR to the development of cryptopatches (CP), aggregates of T cell precursors in the **mouse** small intestine. **Mice** genetically deficient in LTalpha or LTbetaR lacked CP. Bone marrow from LTalpha-deficient **mice** was unable to initiate development of CP or isolated lymphoid follicles (ILF) after transfer to CD132-null **mice** lacking CP and ILF. However, LTalpha-deficient bone marrow-derived cells contributed to CP formed in CD132-null **mice** receiving a mixture of wild-type and LTalpha-deficient bone marrow cells. Transfer of wild-type bone marrow into irradiated LTalpha-deficient **mice** resulted in reconstitution of both CP and ILF. However, the LT-dependent formation of CP was distinguished from the LT-dependent formation of ILF and Peyer's patches by not requiring the presence of an intact NF-kappaB-inducing **kinase** gene. CP but not ILF were present in the small intestine from NF-kappaB-inducing **kinase** -deficient alymphoplasia **mice**, indicating that the alternate NF-kappaB activation pathway required for other types of LTbetaR-dependent lymphoid organogenesis is dispensable for CP development. In addition, we identified VCAM-1(+) cells within both CP and ILF that are candidates for the **stromal cells** involved in receiving LT-dependent signals from the hemopoietic precursors recruited to CP. These findings demonstrate that interactions between cells expressing LTalpha(1)beta(2) and LTbetaR are a shared feature in the development of all small intestinal lymphoid aggregates.

L19 ANSWER 6 OF 27 MEDLINE on STN
ACCESSION NUMBER: 2004572999 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15492752
TITLE: Acquisition of **lymph node**, but not distant metastatic potentials, by the overexpression of CXCR4 in human oral squamous cell carcinoma.
AUTHOR: Uchida Daisuke; Begum Nasima-Mila; Tomizuka Yoshifumi; Bando Takashi; Almofti Ammar; Yoshida Hideo; Sato Mitsunobu
CORPORATE SOURCE: Second Department of Oral and Maxillofacial Surgery, Tokushima University School of Dentistry, Kuramoto, Tokushima, Japan.. daisuke@dent.tokushima-u.ac.jp
SOURCE: Laboratory investigation; a journal of technical methods and pathology, (2004 Dec) 84 (12) 1538-46.
Journal code: 0376617. ISSN: 0023-6837.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20041117
Last Updated on STN: 20050422
Entered Medline: 20050421

AB Recently, it has been suggested that chemokine/receptor interactions determine the destination of the invasive tumor cells in several types of cancer. It has also been proposed that the **stromal cell** -derived factor-1 (SDF-1; CXCL12)/CXCR4 system might be involved **lymph node** metastasis in oral squamous cell carcinoma (SCC). In order to further clarify the role of the SDF-1/CXCR4 system in oral SCC, we generated CXCR4 stable transfectants (IH-CXCR4) using oral SCC cells, and compared them to IH, which did not express CXCR4 and which did not have **lymph node** metastatic potentials in vivo. We introduced enhanced green fluorescent protein (GFP) fused-CXCR4 into IH cells, and detected the GFP fluorescence in the cytoplasm and cell membrane in approximately 60% of the G418-resistant cells. This bulk-transfectant expressed a high level of CXCR4 mRNA and protein, and exhibited the characteristic calcium fluxes and chemotactic activity observed in treatment with SDF-1. SDF-1 biphasically activated extracellular signal-regulated **kinase** (ERK)1/2, but continuously activated Akt/protein **kinase** B (PKB) in IH-CXCR4 cells. Most importantly, IH-CXCR4 cells frequently metastasized to the cervical **lymph node**, but not to the distant organs in the orthotopic inoculation of nude **mice**. Furthermore, these **lymph node** metastases were inhibited by the treatment of a mitogen-activated protein **kinase**/ERK **kinase** inhibitor, U0126, or a phosphatidylinositol 3 **kinase** inhibitor, wortmannin. These results indicate that SDF-1/CXCR4 signaling mediates the establishment of **lymph node** metastasis in oral SCC via ERK1/2 or Akt/PKB pathway.

L19 ANSWER 7 OF 27 MEDLINE on STN
ACCESSION NUMBER: 2004286637 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15186750
TITLE: Requirement for Tec **kinases** in chemokine-induced migration and activation of Cdc42 and Rac.
AUTHOR: Takesono Aya; Horai Reiko; Mandai Michiko; Dombroski Derek; Schwartzberg Pamela L
CORPORATE SOURCE: National Human Genome Research Institute, National Institutes of Health, Bethesda, MD 20892, USA.
SOURCE: Current biology : CB, (2004 May 25) 14 (10) 917-22. Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040610
Last Updated on STN: 20040721
Entered Medline: 20040720

AB Cell polarization and migration in response to chemokines is essential for proper development of the immune system and activation of immune responses. Recent studies of chemokine signaling have revealed a critical role for PI3-**Kinase**, which is required for polarized membrane association of pleckstrin homology (PH) domain-containing proteins and activation of Rho family GTPases that are essential for cell polarization and actin reorganization. Additional data argue that tyrosine **kinases** are also important for chemokine-induced Rac activation. However, how and which **kinases** participate in these pathways remain unclear. We demonstrate here that the Tec **kinases** Itk and Rlk play an important role in chemokine signaling in T lymphocytes. Chemokine stimulation induced transient membrane association of Itk and

phosphorylation of both Itk and Rlk, and purified T cells from Rlk(-/-)Itk(-/-) **mice** exhibited defective migration to multiple chemokines in vitro and decreased homing to **lymph nodes** upon transfer to wt **mice**. Expression of a dominant-negative Itk impaired SDF-1alpha-induced migration, cell polarization, and activation of Rac and Cdc42. Thus, Tec **kinases** are critical components of signaling pathways required for actin polarization downstream from both antigen and chemokine receptors in T cells.

L19 ANSWER 8 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:288935 BIOSIS
DOCUMENT NUMBER: PREV200400287692
TITLE: Differential TNFR and LT beta R regulation of High Endothelial Venule (HEV) Specific Genes.
AUTHOR(S): Liao, Shan [Reprint Author]; Lesslauer, Werner; Ruddle, Nancy H
CORPORATE SOURCE: Epidemiology and Public Health, Yale University School of Medicine, 60 College Street, New Haven, CT, 06520-8034, USA shan.liao@yale.edu
SOURCE: FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst. 332.1. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia, USA. April 17-21, 2004. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jun 2004
Last Updated on STN: 16 Jun 2004

AB HEVs are specialized **lymph node** blood vessels where lymphocyte trafficking occurs. Optimal HEV function may be regulated at the level of gene expression of glycoproteins (GlyCAM-1, MAdCAM-1), chemokines (SLC) and posttranslational modifying enzymes (FucTIV, FucTVII, and an HEV specific GlcNAc-6-sulfotransferase (HEC-6ST)). We have previously determined that LTbR signaling contributes to HEV and HEC6ST in LTb-/- and in RIPLTab transgenic **mice**. Both the classical and alternative NF-kB pathways have been implicated in LTbR signal transduction in fibroblasts and spleen cells. However, it was not clear whether LTab could directly stimulate endothelial cells and/or whether its effect was mediated through **stromal cells**, which in turn activate HEV gene expression. Endothelial cell lines, bEND.3 and SVEC, were adopted as an in vitro system to evaluate and compare LTbR and TNFR mediated signaling for endothelial and HEV specific genes. FACS analysis revealed LTbR surface expression on both cell lines. Several genes were differentially induced by treatment with LTbR agonistic antibody or TNF. The signaling pathways regulating gene expression also differed as revealed by treatment with **kinase** or NF-kB inhibitors. Therefore, LTab has the capacity to directly activate endothelial cells and the pathways and genes differ from those employed by TNF. Supported by NIH CA16885 and the Anna Fuller Fund for Cancer Research.

L19 ANSWER 9 OF 27 MEDLINE on STN
ACCESSION NUMBER: 2003561148 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14633723
TITLE: Both hepatocyte growth factor (HGF) and stromal-derived factor-1 regulate the metastatic behavior of human rhabdomyosarcoma cells, but only HGF enhances their resistance to radiochemotherapy.
AUTHOR: Jankowski Kacper; Kucia Magda; Wysoczynski Marcin; Reca Ryan; Zhao Dongling; Trzyna Ela; Trent John; Peiper Stephen; Zembala Marek; Ratajczak Janina; Houghton Peter;

Janowska-Wieczorek Anna; Ratajczak Mariusz Z
CORPORATE SOURCE: Stem Cell Biology Program, James Graham Brown Cancer Center, University of Louisville, 529 South Jackson Street, Louisville, KY 40202, USA.
CONTRACT NUMBER: 3P0 SE 10122 (NHLBI)
R01 HL 61796-01
SOURCE: Cancer research, (2003 Nov 15) 63 (22) 7926-35.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20031216
Last Updated on STN: 20040210
Entered Medline: 20040209

AB Rhabdomyosarcomas (RMSs) are frequently characterized by bone marrow involvement. Recently, we reported that human RMS cells express the CXC chemokine receptor-4 (CXCR4) and postulated a role for the CXCR4 stromal-derived factor (SDF)-1 axis in the metastasis of RMS cells to bone marrow. Because RMS cells also express the tyrosine **kinase** receptor c-MET, the specific ligand hepatocyte growth factor (HGF) that is secreted in bone marrow and **lymph node** stroma, we hypothesized that the c-MET-HGF axis modulates the metastatic behavior of RMS cells as well. Supporting this concept is our observation that conditioned media harvested from expanded ex vivo human bone marrow fibroblasts chemoattracted RMS cells in an HGF- and SDF-1-dependent manner. Six human alveolar and three embryonal RMS cell lines were examined. We found that although HGF, similar to SDF-1, did not affect the proliferation of RMS cells, it induced in several of them: (a) locomotion; (b) stress fiber formation; (c) chemotaxis; (d) adhesion to human umbilical vein endothelial cells; (e) trans-Matrigel invasion and matrix metalloproteinase secretion; and (f) phosphorylation of mitogen-activated protein **kinase** p42/44 and AKT. Moreover HGF, but not SDF-1, increased the survival of RMS cells exposed to radio- and chemotherapy. We also found that the more aggressive alveolar RMS cells express higher levels of c-MET than embryonal RMS cell lines and "home/seed" better into bone marrow after i.v. injection into immunocompromised **mice**. Because we could not find any activating mutations in the **kinase** region of c-MET or any evidence for HGF autocrine stimulation, we suggest that the increased response of RMS cell lines depends on overexpression of functional c-MET. We conclude that HGF regulates the metastatic behavior of c-MET-positive RMS cells, directing them to the bone marrow and **lymph nodes**. Signaling from the c-MET receptor may also contribute to the resistance of RMS cells to conventional treatment modalities.

L19 ANSWER 10 OF 27 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-00219 BIOTECHDS
TITLE: Suppression of met expression: A possible cancer treatment; potential prostate cancer gene therapy involving use of ribozyme against receptor protein-tyrosine-**kinase**
AUTHOR: SHINOMIYA N; WOUDE GFV
CORPORATE SOURCE: Van Andel Res Inst
LOCATION: Shinomiya N, Van Andel Res Inst, Oncol Mol Lab, 333 Bostwick NE, Grand Rapids, MI 49503 USA
SOURCE: CLINICAL CANCER RESEARCH; (2003) 9, 14, 5085-5090
ISSN: 1078-0432
DOCUMENT TYPE: Journal
LANGUAGE: English

AB DERWENT ABSTRACT: Met is a receptor protein-tyrosine-**kinase** (EC-2.7.1.112) and the only known receptor for HGF/SF. This ligand/receptor signaling pair mediates a vast range of biological

activities not only in normal organ development and physiological functions but also in tumor proliferation, progression, invasion, and metastasis. Tumor cells that express high levels of Met molecules on their surface are more malignant and metastatic. In many carcinomas, HGF/SF acting in a paracrine manner is produced by **stromal cells** adjacent to the tumor. Inhibition of Met expression suppresses the malignant progression of tumor cells. A ribozyme strategy has been used to suppress the growth of human glioblastorna tumors. Because overexpression of Met receptors is observed in a wide spectrum of carcinomas and considered to play a key role in the progression of cancer cells, targeting of this molecule could become one of the most useful. treatment modalities for refractory cancers. Molecular targeting of the Met signaling pathways by using specifically designed genes. which target c-met, can be used as a treatment modality for controlling tumor growth and metastasis. An adeno virus vector expressing c-Met ribozyme inhibits tumorigenicity and **lymph node** metastasis of human prostate cancer cells by using an orthotopically implanted in vivo **mouse** model. In prostate cancer cells especially, high expression of Met is associated with resistance against chemotherapy including hormonal therapy and is often observed in the advanced stages of clinical cases. By reducing Met expression using a ribozyme that targets Met mRNA, tumor growth and **lymph node** metastasis were dramatically inhibited(6 pages)

L19 ANSWER 11 OF 27 MEDLINE on STN
ACCESSION NUMBER: 2003543598 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12881311
TITLE: Complexity within the plasma cell compartment of **mice** deficient in both E- and P-selectin: implications for plasma cell differentiation.
AUTHOR: Underhill Gregory H; Kolli K Pallav; Kansas Geoffrey S
CORPORATE SOURCE: Department of Microbiology-Immunology, Northwestern Medical School, 303 E Chicago Ave, Chicago, IL 60611, USA.
CONTRACT NUMBER: HL58710 (NHLBI)
SOURCE: Blood, (2003 Dec 1) 102 (12) 4076-83. Electronic Publication: 2003-07-24.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20031119
Last Updated on STN: 20040115
Entered Medline: 20040114

AB Antibody-secreting plasma cells represent the critical end-stage effector cells of the humoral immune response. Here, we show that several distinct plasma cell subsets are concurrently present in the **lymph nodes**, spleen, and bone marrow of **mice** deficient in both E- and P-selectin. One of these subsets was a B220-negative immunoglobulin g (IgG) plasma cell population expressing low to negative surface levels of syndecan-1. Examination of the chemotactic responsiveness of IgG plasma cell subsets revealed that migration toward **stromal cell**-derived factor 1/CXC ligand 12 (SDF-1/CXCL12) was primarily limited to the B220-lo subset regardless of tissue source. Although B220-negative plasma cells did not migrate efficiently in response to CXCL12 or to other chemokines for which receptor mRNA was expressed, these cells expressed substantial surface CXC chemokine receptor-4 (CXCR4), and CXCL12 stimulation rapidly induced extracellular signal regulated **kinase** 1 (ERK1)/ERK2 phosphorylation, demonstrating that CXCR4 retained signaling capacity. Therefore, B220-negative plasma cells exhibit a selective uncoupling of chemokine receptor expression and signaling from migration. Taken

together, our findings document the presence of significant heterogeneity within the plasma cell compartment, which suggests a complex step-wise scheme of plasma cell differentiation in which the degree of differentiation and tissue location can influence the chemotactic responsiveness of IgG plasma cells.

L19 ANSWER 12 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:153519 BIOSIS
DOCUMENT NUMBER: PREV200400148159
TITLE: Roles of PLC-beta2, -beta3, and PI3K in T-cell migration to SDF 1-alpha.
AUTHOR(S): Bach, Tami L. [Reprint Author]; Chen, Qing-Min [Reprint Author]; Jordan, Martha S.; Wu, Dianqing; Zigmond, Sally H.; Abrams, Charles S. [Reprint Author]
CORPORATE SOURCE: Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 768a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB Chemokines bind G-protein coupled receptors and play an essential role in both the immune and inflammatory responses. In T lymphocytes, little is known about the signaling pathways required for chemokine-mediated cell migration. Phospholipase C (PLC) and phosphatidylinositol 3-**kinase** (PI3K) are two distinct signaling molecules that have been proposed as potential candidates in the regulation of this process. Studies with knockout **mice** have demonstrated a critical role for D3-phosphoinositide production by PI3Kgamma in Galphai-coupled receptor-mediated neutrophil chemotaxis. Similar studies have failed to demonstrate a role for IP3 or DAG production by PLCbeta in this neutrophil response. In the current investigation, peripheral T-cells were isolated from the **lymph nodes** of wild type **mice** and **mice** with loss-of-function mutations of either PI3Kgamma, or both of the two dominant lymphocyte PLCbeta isoforms (PLCbeta2 and PLCbeta3). Using a transwell assay, migration of lymphocytes toward SDF-1alpha (37.5 nM) was quantitated after 3 hours, the time point at which migration was maximal for both wild type and knockout T-cells. We found that lymphocytes isolated from wild type **mice** exhibited an eighteen-fold increase in migration with SDF-1alpha stimulation compared to baseline. In contrast, loss of either PLCbeta2beta3 or PI3Kgamma decreased chemokine-stimulated T-cell migration by 68%+-14% ($p<0.005$) and 12+-4% ($p<0.5$), respectively. The impaired sensitivity of the PLCbeta2/beta3-null T-cells occurred over a wide range of agonist, and in contrast to wild type lymphocytes, a large percentage of migration in the PLCbeta2/beta3-null T-cells was due to SDF-induced chemokinesis and not chemotaxis. Chelation of intracellular calcium by BAPTA (30 nM) decreased the chemotactic response of wild type lymphocytes, but pharmacologic inhibition of PKC isoforms by GF109203x (5 muM) or Go 6976 (5 muM) did not impair T-cell migration. Furthermore, SDF-1alpha-induced calcium efflux was not detected in the PLCbeta2beta3-null lymphocytes. This suggests that the T-cell migration defect seen in the PLCbeta2/beta3-null T-cells may be due to an impaired ability to increase intracellular calcium, while there appears to be little requirement for the stimulation of PKC. We have also found that inhibition of PI3K by either wortmannin (100 nM) or

LY294002 (50 muM), decreased SDF-1alpha-induced migration of wild type cells to near baseline, suggesting that PI3K does contribute to T-cell migration, but the PI3Kgamma isoform contributes relatively little to this process. These results show that in vivo phospholipid second messengers generated by PLCbeta and isoforms of PI3K, other than PI3Kgamma, play a critical role in lymphocyte chemotaxis. Our data demonstrate that although PLCbeta-mediated signaling plays no role in neutrophil chemotaxis, it makes a substantial contribution to this process within T lymphocytes.

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ACCESSION NUMBER: 2003:451651 BIOSIS
DOCUMENT NUMBER: PREV200300451651
TITLE: Involvement of **stromal cell**-derived factor-1/CXCR4 signaling in **lymph node** metastasis of oral squamous cell carcinoma.
AUTHOR(S): Uchida, Daisuke [Reprint Author]; Begum, Nasima-Mila; Almofti, Ammar; Kawamata, Hitoshi; Nakashiro, Koh-Ichi; Tateishi, Yoshihisa; Hamakawa, Hiroyuki; Yoshida, Hideo; Sato, Mitsunobu
CORPORATE SOURCE: 2nd Dept. Oral and Maxillofacial Surgery, School of Dentistry, Tokushima University, Tokushima, Japan
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (July 2003) Vol. 44, pp. 452. print. Meeting Info.: 94th Annual Meeting of the American Association for Cancer Research. Washington, DC, USA. July 11-14, 2003. ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Oct 2003 Last Updated on STN: 1 Oct 2003

L19 ANSWER 14 OF 27 MEDLINE on STN

ACCESSION NUMBER: 2003491192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14567988
TITLE: Possible role of **stromal-cell**-derived factor-1/CXCR4 signaling on **lymph node** metastasis of oral squamous cell carcinoma.
AUTHOR: Uchida Daisuke; Begum Nasima Mila; Almofti Ammar; Nakashiro Koh-ichi; Kawamata Hitoshi; Tateishi Yoshihisa; Hamakawa Hiroyuki; Yoshida Hideo; Sato Mitsunobu
CORPORATE SOURCE: Second Department of Oral and Maxillofacial Surgery, Tokushima University School of Dentistry, 3-18-15 Kuramoto, Tokushima 770-8504, Japan.. daisuke@dent.tokushima-u.ac.jp
SOURCE: Experimental cell research, (2003 Nov 1) 290 (2) 289-302. Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031022 Last Updated on STN: 20031219 Entered Medline: 20031202

AB We examined the role of chemokine signaling on the **lymph node** metastasis of oral squamous cell carcinoma (SCC) using **lymph node** metastatic (HNt and B88) and nonmetastatic oral SCC cells. Of 13 kinds of chemokine receptors examined, only CXCR4 expression was up-regulated in HNt and B88 cells. CXCR4 ligand, **stromal-cell**-derived factor-1alpha (SDF-1alpha; CXCL12),

induced characteristic calcium fluxes and chemotaxis only in CXCR4-expressing cells. CXCR4 expression in metastatic cancer tissue was significantly higher than that in nonmetastatic cancer tissue or normal gingiva. Although SDF-1alpha was undetectable in either oral SCC or normal epithelial cells, submandibular **lymph nodes** expressed the SDF-1alpha protein, mainly in the **stromal cells**, but occasionally in metastatic cancer cells. The conditioned medium from lymphatic **stromal cells** promoted the chemotaxis of B88 cells, which was blocked by the CXCR4 neutralization. SDF-1alpha rapidly activated extracellular signal-regulated **kinase** (ERK)1/2 and Akt/protein **kinase** B (PKB), and their synthetic inhibitors attenuated the chemotaxis by SDF-1alpha. SDF-1alpha also activated Src family **kinases** (SFKs), and its inhibitor PP1 diminished the SDF-1alpha-induced chemotaxis and activation of both ERK1/2 and Akt/PKB. These results indicate that SDF-1/CXCR4 signaling may be involved in the establishment of **lymph node** metastasis in oral SCC via activation of both ERK1/2 and Akt/PKB induced by SFKs.

L19 ANSWER 15 OF 27 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:215250 SCISEARCH
THE GENUINE ARTICLE: 649WP
TITLE: Phase I dose escalation clinical trial of adenovirus vector carrying osteocalcin promoter-driven herpes simplex virus thymidine **kinase** in localized and metastatic hormone-refractory prostate cancer
AUTHOR: Kubo H; Gardner T A; Wada Y; Koeneman K S; Gotoh A; Yang L; Kao C H; Lim S D; Amin M B; Yang H; Black M E; Matsubara S; Nakagawa M; Gillenwater J Y; Zhau H Y E; Chung L W K (Reprint)
CORPORATE SOURCE: Emory Univ, Sch Med, Winship Canc Inst, Dept Urol, Mol Urol & Therapeut Program, 1365-B Clifton Rd, Room B5101, Atlanta, GA 30322 USA (Reprint); Emory Univ, Sch Med, Winship Canc Inst, Dept Urol, Mol Urol & Therapeut Program, Atlanta, GA 30322 USA; Indiana Univ, Med Ctr, Dept Urol, Indianapolis, IN 46202 USA; Kobe Univ, Sch Med, Dept Urol, Kobe, Hyogo 6500017, Japan; Univ Virginia Hlth Syst, Dept Urol, Charlottesville, VA 22908 USA; Emory Univ, Sch Med, Dept Pathol & Lab Med, Atlanta, GA 30322 USA; Washington State Univ, Dept Pharmaceut Sci, Pullman, WA 99164 USA; Kagoshima Univ, Fac Med, Dept Urol, Kagoshima 8908506, Japan
COUNTRY OF AUTHOR: USA; Japan
SOURCE: HUMAN GENE THERAPY, (FEB 2003) Vol. 14, No. 3, pp. 227-241

Publisher: MARY ANN LIEBERT INC PUBL, 2 MADISON AVENUE, LARCHMONT, NY 10538 USA.
ISSN: 1043-0342.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 42

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Osteocalcin (OC), a major noncollagenous bone matrix protein, is expressed prevalently in prostate cancer epithelial cells, adjacent fibromuscular **stromal cells**, and osteoblasts in locally recurrent prostate cancer and prostate cancer bone metastasis [Matsubara, S., Wada, Y., Gardner, T. A., Egawa, M., Park, M. S., Hsieh, C. L., Zhau, H. E., Kao, C., Kamidono, S., Gillenwater, J.Y., and Chung, L. W. (2001). Cancer Res. 61, 6012-6019]. We constructed an adenovirus vector carrying osteocalcin promoter-driven herpes simplex virus thymidine **kinase** (Ad-OC-hsv-TK) to cotarget prostate cancer cells and their surrounding **stromal cells**. A phase I dose escalation

clinical trial of the intralesional administration of Ad-OC-hsv-TK followed by oral valacyclovir was conducted at the University of Virginia (Charlottesville, VA) in 11 men with localized recurrent and metastatic hormone-refractory prostate cancer (2 local recurrent, 5 osseous metastasis, and 4 **lymph node** metastasis) in order to determine the usefulness of this vector for the palliation of androgen-independent prostate cancer metastasis. This is the first clinical trial in which therapeutic adenoviruses are injected directly into prostate cancer **lymph node** and bone metastasis. Results show that (1) all patients tolerated this therapy with no serious adverse events; (2) local cell death was observed in treated lesions in seven patients (63.6%) as assessed by TUNEL assay, and histomorphological change (mediation of fibrosis) was detected in all posttreated specimens; (3) one patient showed stabilization of the treated lesion for 317 days with no alternative therapy. Of the two patients who complained of tumor-associated symptoms before the treatment, one patient with bone pain had resolution of pain, although significant remission of treated lesions was not observed by image examination; (4) CD8-positive T cells were predominant compared with CD4-positive T cells, B cells (L26 positive), and natural killer cells (CD56 positive) in posttreated tissue specimens; (5) levels of HSV TK gene transduction correlated well with coxsackie-adenovirus receptor expression but less well with the titers of adenovirus injected; and (6) intrinsic OC expression and the efficiency of HSV TK gene transduction affected the levels of HSV TK protein expression in clinical specimens. Our data suggest that this form of gene therapy requires further development for the treatment of androgen-independent prostate cancer metastasis although histopathological and immunohistochemical evidence of apoptosis was observed in the specimens treated. Further studies including the development of viral delivery will enhance the efficacy of Ad-OC-hsv-TK.

L19 ANSWER 16 OF 27 MEDLINE on STN

ACCESSION NUMBER:	2003003088 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 12393730
TITLE:	CCR7-mediated physiological lymphocyte homing involves activation of a tyrosine **kinase** pathway.
AUTHOR:	Stein Jens V; Soriano Silvia F; M'rini Christine; Nombela-Arrieta Cesar; de Buitrago Gonzalo Gonzalez; Rodriguez-Frade Jose Miguel; Mellado Mario; Girard Jean-Philippe; Martinez-A Carlos
CORPORATE SOURCE:	Department of Immunology and Oncology, Centro Nacional de Biotecnologia/Consejo Superior de Investigaciones Cientificas (CSIC), Madrid, Spain.. jstein@cnb.uam.es
SOURCE:	Blood, (2003 Jan 1) 101 (1) 38-44. Electronic Publication: 2002-06-28. Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:	200303
ENTRY DATE:	Entered STN: 20030103 Last Updated on STN: 20030331 Entered Medline: 20030318

AB Homing of blood-borne lymphocytes to peripheral **lymph nodes** (PLNs) is a multistep process dependent on the sequential engagement of L-selectin, which mediates lymphocyte rolling along the luminal surface of high endothelial venules (HEVs), followed by activation of lymphocyte integrins and transmigration through HEVs. Within lymphoid tissue, B and T lymphocytes then migrate toward specific microenvironments such as B-cell follicles and the paracortex, respectively. The lymphocyte-expressed chemokine receptor CCR7 is playing an important role during this process, as its HEV-presented ligands CCL19 and CCL21 can

trigger rapid integrin activation under flow in addition to inducing a chemotactic response, which may participate in transmigration and/or interstitial migration. Here, we report that Tyrphostin (Tyr) AG490, a pharmacological inhibitor of Janus family tyrosine **kinases** (Jaks), blocked the chemotactic response of primary **mouse** lymphocytes to CCL19 and CCL21 in a dose-dependent manner. Furthermore, Tyr AG490 inhibited rapid CCL21-mediated up-regulation of alpha4 and beta2 integrin adhesiveness in static adhesion assays and under physiological flow, whereas adhesion induced by phorbol myristate acetate remained unaltered. Using intravital microscopy of subiliac PLNs in **mice** , we found that adoptively transferred Tyr AG490-treated lymphocytes adhered significantly less in HEVs compared with control cells, although L-selectin-mediated rolling was similar in both samples. Finally, we observed rapid Jak2 phosphorylation in CCL21-stimulated primary **mouse** lymphocytes. Thus, our study suggests a role for Jak tyrosine **kinases** during CCR7-mediated lymphocyte recirculation.

L19 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:120036 HCAPLUS
DOCUMENT NUMBER: 138:236622
TITLE: RelB in secondary lymphoid organ development: differential regulation by lymphotoxin and tumor necrosis factor signaling pathways
AUTHOR(S): Yilmaz, Z. Buket
CORPORATE SOURCE: Institut fuer Toxikologie und Genetik, Germany
SOURCE: Wissenschaftliche Berichte - Forschungszentrum Karlsruhe (2002), FZKA 6793, i-xv, 1-117
CODEN: WBFKF5; ISSN: 0947-8620
DOCUMENT TYPE: Report
LANGUAGE: English

AB Primary lymphoid organs are the major sites of lymphopoiesis where lymphocytes proliferate and mature into functional but naive cells. Secondary lymphoid organs are sites where these lymphocytes encounter antigens and elicit immune responses. RelB is a member of the Rel/NF-κB family of inducible dimeric transcription factors. RelB is abundantly expressed in secondary lymphoid organs, such as spleen, **lymph nodes**, and Peyer's patches (PP). RelB-deficient **mice** have improper spleen structure and lack organizing centers for PPs, defects that can not be restored by the adoptive transfer of wild-type bone marrow cells. The work presented here revealed a reduction in expression of the homing chemokines B lymphocyte chemoattractant (BLC) and secondary lymphoid organ chemokine (SLC) in RelB-deficient spleen, suggesting a role for RelB in proper expression of chemokines by splenic **stromal cells**. Moreover, interleukin-7 (IL-7)-induced expression of lymphotoxin (LT) in intestinal cells, a crucial step in early PP development, was not impaired in RelB-deficient embryos, suggesting functional hematopoietic inducers and a defect in LTβ receptor (LTβR) expressing stromal responders. Activation of LTβR signaling in fibroblasts resulted in the specific induction of p52-RelB heterodimers, while tumor necrosis factor (TNF) induced classical p50-RelA NF-κB complexes. LTβR-induced RelB nuclear translocation and DNA binding of p52-RelB heterodimers required the degradation of the inhibitory p52 precursor, p100, which was dependent on the IκB **kinase** (IKK) complex subunit IKKα, but not on IKKβ or IKKγ. In contrast to LTβR signaling, TNFR signaling increased p100 and RelB levels both in cytoplasm and nucleus and RelB was bound to p100 in both compartments. Despite the abundant presence of RelB in the nucleus, RelB DNA binding was almost undetectable in TNF treated fibroblasts. Forced expression of p50 and p52 could not rescue the lack of DNA binding. In contrast, RelB DNA binding increased in cells lacking the C-terminus of p100, but not of p105, strongly

suggesting that it is the specific inhibitory function of the C-terminal domain of p100, rather than the lack of the heterodimerization partner, which prevents RelB DNA binding in TNF-stimulated fibroblasts. Thus, RelB and p52 in **stromal cells** could function in the proper development of the spleen by regulating the expression of chemokines such as BLC. Furthermore, generation of p52-RelB heterodimers by the LTβR pathway involving p100 degradation, appears to be a critical step in the formation of PP anlage.

REFERENCE COUNT: 118 THERE ARE 118 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 12:14:19 ON 10 JUN 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 12:14:46 ON 10 JUN 2005

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L1      1324738 S KINASE?
L2       395747 S LYMPH(A)NODE
L3        68040 S STROMAL(W)CELL
L4         5495 S L1 AND L2
L5          102 S L3 AND L4
L6      7110172 S CLON? OR EXPRESS? OR RECOMBINANT
L7           95 S L5 AND L6
L8           50 DUP REM L7 (45 DUPLICATES REMOVED)
L9      3990560 S MURINE OR MOUSE
L10           0 S L2(A)L3(A)L1
L11        1624 S L4 AND L9
L12          53 S L3 AND L11
L13          27 DUP REM L12 (26 DUPLICATES REMOVED)
                E BIRD T A/AU
L14         197 S E3
                E VIRCA G D/AU
L15         131 S E3
                E ANDERSON D M/AU
L16        1948 S E3
L17        2268 S L13 OR L14 OR L15 OR L16
L18          27 S L5 AND L17
L19          27 DUP REM L18 (0 DUPLICATES REMOVED)
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